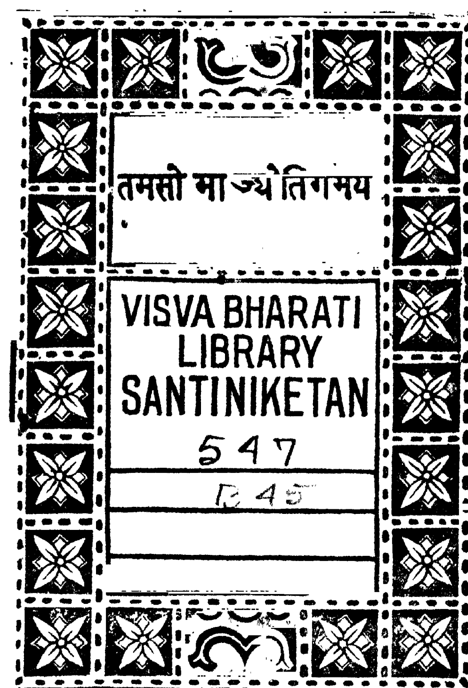


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A TEXTBOOK OF ORGANIC CHEMISTRY

BY

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Companion Volume

Practical Organic Chemistry

By J. J. Sudborough, Ph.D., D.Sc., F.I.C., and T. Campbell James, D.Sc., F.I.C., Professor of Chemistry in the University College of Wales, Aberystwyth. Illustrated.

Nature: "Altogether the book is probably the most complete among those of home manufacture on the subject that has yet appeared"

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PREFACE TO THE 1922 EDITION

The present edition of *Bernthsen's Organic Chemistry*, while based upon former editions, consists of a complete revision with the addition of a large amount of new material. The earlier chapters give an outline of General Systematic Organic Chemistry, and the succeeding ones deal in rather more detail with the chief problems which have attracted the attention of chemists during recent years.

The material retained from previous editions has been carefully reconsidered and modified to bring it into accordance with the results of recent research. To the subject-matter dealt with in those editions the following chapters have now been added: *LII. Some Cyclic Systems; LIII. Organic Derivatives of Arsenic; LIV. Synthetic Drugs; LV. Synthetic Dyes; LVI. The Chemistry of Rubber.*

The last four chapters indicate the application of organic chemistry to technical and commercial problems, and should be of particular practical value to the present-day student.

Numerous references to original papers are given in the text. The following works are recommended for special study:—

Meyer and Jacobson, *Handbuch der organischen Chemie*; Lassar-Cohn, *Arbeitsmethoden*; Th. Weyl, *Die Methoden der organischen Chemie*; Werner, *Lehrbuch der Stereochemie*; Landolt, *Das optische Drehungsvermögen*; O. Aschan, *Chemie der alicyclischen Verbindungen*; E. Fischer, *Aminosäuren und Polypeptide*, 1906; *Purin Gruppe*, 1907; *Kohlenhydrate und Fermente*, 1909; Cain, *The Diazo-compounds*; Smiles, *Relations between Chemical Constitution and Physical Properties*; Stewart, *Stereo-chemistry*; *Recent Advances in Organic Chemistry*;

Sidgwick, *Organic Chemistry of Nitrogen*; Harden, *Alcoholic Fermentation*; E. F. Armstrong, *Simple Carbohydrates and Glucosides*; Bayliss, *Enzyme Action*; Schryver, *Proteins*; Cain and Thorpe, *Synthetic Dyestuffs*; Cain, *The Manufacture of Intermediate Products for Dyes*; P. May, *Synthetic Drugs*; Harries, *Untersuchungen über das Ozon und seine Einwirkung auf organische Verbindungen*; Hale, *Synthetic Use of Metals in Organic Chemistry*; also various volumes in Sir Edward Thorpe's *Monographs on Industrial Chemistry*, e.g. Morgan's *Organic Derivatives of Arsenic and Antimony*; Watson's *Colour in Relation to Chemical Constitution*; Perkin and Everest's *Natural Organic Colouring Matters*; Henderson's *Catalysis in Industrial Chemistry*.

Valuable Summaries of certain fields of Organic Work, such as Combustion, Diazo-compounds, Grignard's Reagents, Camphor, Tautomerism, Stereo-chemistry of Nitrogen, &c., will be found in the Reports of the British Association since 1900, and also in Ahren's *Sammlung chemischer und chem.-technischer Vorträge* from 1897 onwards.

J. J. SUDBOROUGH.

BANGALORE, *October, 1921.*

ABBREVIATIONS

A. = Liebig's *Annalen der Chemie.*
Abs. = *Journal of the Chemical Society.* Abstracts.
Am. = *American Chemical Journal.*
Am. J. Pharm. = *American Journal of Pharmacy.*
Annales = *Annales de Chimie et de Physique.*
Arch. f. Phys. = *Archiv für Physiologie.*
Arch. Pharm. = *Archiv der Pharmacie.*
B. = *Berichte der deutschen chemischen Gesellschaft.*
B. A. Rep. = *British Association Report.*
B. bot. Ges. = *Berichte der deutschen botanischen Gesellschaft.*
Bio. J. = *Biochemical Journal.*
Bio. Z. = *Biochemische Zeitschrift.*
Bull Soc. = *Bulletin de la Société chimique de France.*
Bull. Soc. Bel. = *Bulletin de la Société chimique de Belgique.*
C. N. = *Chemical News.*
C. R. = *Comptes rendus de l'Académie des Sciences.*
C. W. = *Chemisch Weekblad.*
C. Z. = *Chemisches Zentral-blatt.*
C. Zeit. = *Chemiker Zeitung.*
Chem. Rev. Can. Chem. = *Chemical Review of Canadian Chemistry.*
E. P. = *English Patent.*
Helv. = *Helvetica Chimica Acta.*
I. R. World = *India-rubber World.*
Ind. J. P. = *Indian Journal of Physics.*
J. A. C. S. = *Journal of the American Chemical Society.*
J. biol. C. = *Journal of Biological Chemistry.*
J. C. S. = *Journal of the Chemical Society.* Transactions.
J. I. E. C. = *Journal of Industrial and Engineering Chemistry.*
J. I. I. S. = *Journal of the Indian Institute of Science.*
J. Ind. = *Journal of the Society of Chemical Industry.*
J. ph. Chem. = *Journal of Physical Chemistry.*
J. Pharm. S. J. = *Journal of the Pharmaceutical Society of Japan.*
J. pr. = *Journal für praktische Chemie.*

J. Ph. Chem. = *Journal of Physical Chemistry.*
J. R. S. A. = *Journal of the Royal Society of Arts.*
J. russ. Soc. = *Journal of the Physical and Chemical Society of Russia.*
J. S. Dyers = *Journal of the Society of Dyers and Colourists.*
Koll. = *Kolloid chemische Beihefte.*
M. = *Monatshefte für Chemie.*
P. = *Proceedings of the Chemical Society.*
P. Roy. S. = *Proceedings of the Royal Society.*
P. R. S. A. = *Proceedings of the Royal Society of Arts.*
Phil. Mag. = *Philosophical Magazine.*
Rec. = *Recueil des Travaux chimiques des Pays-Bas.*
Rep. = *Annual Reports on the Progress of Chemistry, Chemical Society.*
S. J. = Sudborough and James's *Practical Organic Chemistry.*
Trans. Far. = *Transactions of the Faraday Society.*
Trans. I. R. I. = *Transactions of the Institution of Rubber Industry.*
Walker, Phys. Chem. = Walker's *Introduction to Physical Chemistry.*
Z. Angew. = *Zeitschrift fur angewandte Chemie.*
Z. Elec. = *Zeitschrift für Elektrochemie.*
Z. phys. = *Zeitschrift für physikalische Chemie.*
Z. physiol. = *Zeitschrift für physiologische Chemie.*

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n = normal.
O-ether = Oxygen ether.
N-ether = Nitrogen ether.
B.-pt. = Boiling-point.
M.-pt. = Melting-point.
d = dextro.
l = lævo.
r = racemic.
s = symmetrical.
i = inactive.
R = alkyl radical.
Me = Methyl, CH_3.
Et = Ethyl, C_2H_5.
Ph = Phenyl, C_6H_5.
o = ortho.
m = meta.
p = para.

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INTRODUCTION

CLASS I.—ALIPHATIC OR OPEN-CHAIN COMPOUNDS

ORGANIC CHEMISTRY

INTRODUCTION

Organic Chemistry is the Chemistry of the Carbon Compounds. Formerly those compounds which occur in the animal and vegetable worlds were classed under Organic, and those which occur in the mineral world under Inorganic Chemistry, the first to adopt this arrangement having been *Léméry* in his Cours de Chimie (1675). After the recognition of the fact that all organic substances contain carbon, it was thought that the difference between organic and inorganic compounds could be explained by saying that the latter were capable of preparation in the laboratory, but the former only in the organism, under the influence of a particular force, the life force—vis vitalis—(*Berzelius*). But this assumption was rendered untenable when *Wöhler* in 1828 synthetically prepared urea, CON_2H_4, a typical secretion of the animal organism, from cyanic acid and ammonia, two compounds which were at that time held to be inorganic; and when, shortly afterwards, the synthesis of acetic acid, by the use of carbon, sulphur, chlorine, water, and zinc, was effected.

Since then so many syntheses of this kind have been achieved as to prove beyond doubt that the same chemical forces act both in the organic and inorganic worlds.

The separation of the two branches, Organic and Inorganic Chemistry, from each other is, however, still retained for convenience sake, although the original reasons for this separation, which at the time was more or less a matter of necessity, have since been found to be erroneous. In consequence of the great capacity of combining with one another which carbon atoms possess, the number of organic compounds is extraordinarily large, and in order to be in a position to study them, it is necessary to have a knowledge of the other elements, including

the metals. The carbon compounds, many of the most important of which contain only carbon and hydrogen, or carbon, hydrogen, and oxygen, also stand in a closer relationship to each other than do the compounds of the other elements. Partly upon grounds of convenience, carbon itself and some of its principal compounds, such as carbonic acid, which is so widely distributed in the mineral kingdom, are treated of under Inorganic Chemistry.

The expressions "organic" and "organized" substances should not be confused; organized substances, *e.g.* leaves, nerves and muscles, and also the life-processes which go on in the interior of the organism, are treated of under Physiology and Bio-chemistry.

Constituents of the Carbon Compounds

Many organic substances are composed of carbon and hydrogen only, and are then termed hydrocarbons, for instance, ethylene, benzene, petroleum, naphthalene, and oil of turpentine; a vast number consist of carbon, hydrogen, and oxygen, for instance, wood spirit, alcohol, glycerine, aldehyde, oil of bitter almonds, formic acid, acetic acid, stearic acid, tartaric acid, benzoic acid, carbolic acid, tannic acid, and alizarin; many compounds contain carbon, hydrogen, and nitrogen, for instance, prussic acid, aniline, and coniine; as examples of compounds containing carbon, hydrogen, nitrogen, and oxygen, may be taken urea, uric acid, indigo, morphine, and quinine. In addition to these, sulphur, chlorine, bromine, iodine, phosphorus, and, generally speaking, the larger number of the more important elements, are also frequent constituents of the carbon compounds.

Qualitative Analysis of Organic Compounds

The presence of **Carbon** in a compound is often proved by the "carbonization" of the latter, *e.g.* starch, sugar, &c., when heated in a glass tube, or when warmed with concentrated sulphuric acid. Carbon compounds which readily volatilize, *e.g.* alcohol, chloroform, acetic acid, do not give these tests, but many of them deposit carbon when their vapours are led through a red-hot tube. The best proof of the presence of carbon is obtained by completely oxidizing the organic compound by either heating it with copper oxide (see below), or

by leading its vapour over the glowing oxide. The carbon present is thus converted into carbon dioxide, and the **Hydrogen** into water.

Nitrogen in organic compounds is recognized—

(*a*) Frequently by a smell resembling that of burnt hair, upon heating;

(*b*) Frequently by the presence of red fumes, or by explosion, upon heating (nitro- and diazo-compounds);

(*c*) In many cases by the liberation of ammonia upon heating with soda-lime (*Wöhler*);

(*d*) In all cases by heating with potassium (and in most cases with sodium), and testing the metallic cyanide formed —(see Cyanogen Compounds)—by dissolving the fused mass in water, adding a few drops of ferrous sulphate solution, boiling, and acidifying with hydrochloric acid (formation of Prussian Blue); or by converting the cyanide into thiocyanate, and proving the presence of the latter by means of the blood-red coloration with ferric chloride. [See tests for hydrocyanic acid (*Lassaigne*).] If sulphur be likewise present, iron filings must be added.

Testing for the **Halogens**. Direct precipitation by nitrate of silver is usually not practicable; thus, no chlorine can be detected in chloroform even upon boiling it with $AgNO_3$. The halogens are therefore tested for:

(*a*) By heating the substance on a platinum wire with cupric oxide in the *Bunsen* flame, or by causing the vapour of the compound to pass over glowing copper gauze; in this way chlorine gives first a blue and then a green flame coloration, and iodine a green (*Beilstein*);

(*b*) By heating the substance strongly with pure lime, and testing the solution of the haloid calcium salt produced with silver nitrate;

(*c*) By heating in a sealed tube with fuming nitric acid and nitrate of silver, when the haloid silver salt is produced (*Carius*).

Testing for **Sulphur**:

(*a*) In many cases, upon boiling with an alkaline solution of lead oxide, brown sulphide of lead is formed (*e.g.* white of egg);

(*b*) By heating with sodium, and testing the resulting sodium sulphide with water upon a silver coin (black stain); or by means of sodium nitroprusside solution (purple-violet coloration) (*Schönn*);

(*c*) By complete oxidation in the dry way, by fusing with potassium carbonate and nitre, or by heating with mercuric oxide and sodium carbonate; or in the wet way, by fuming nitric acid (*Carius*), and testing the sulphuric acid produced, by barium chloride solution.

In like manner **Phosphorus** is converted by complete oxidation into phosphoric acid; or, upon heating with powdered magnesia, and moistening the resulting mass with water, the presence of phosphuretted hydrogen can be recognized (*Schönn*).

All the **other Elements** are tested for, after complete oxidation of the compound (preferably by *Carius'* method), in the usual way.

Another method (B. 1904, **37**, 2155) is to heat a small amount of the substance with sodium peroxide and twenty-five times its weight of naphthalene or cinnamic acid in an iron tube, and then test for haloids, sulphates, phosphates, &c.

Quantitative Organic or Elementary Analysis

Estimation of Carbon and Hydrogen (Combustion). The substance is oxidized by heating it to redness with cupric oxide (*Liebig*), or with other substances which readily give up oxygen, such as lead chromate, platinum and oxygen (*Dennstedt*),* &c., in a tube of difficultly fusible glass which is open either at one or at both ends.

The carbon dioxide, thus produced by the oxidation of the carbon, is absorbed by a concentrated solution of caustic potash contained in specially shaped bulbs,* and the water, produced by the oxidation of the hydrogen, in a **U**-shaped calcic chloride tube, both tubes being weighed before and after the combustion. If the substance—(0·2 to 0·3 grm.)—is solid, it is either mixed with fine, dry copper oxide (*Liebig*, *Bunsen*), or placed in a porcelain or platinum boat and burnt in a stream of air or oxygen (open tube). Liquids are weighed out in small tubes or thin sealed glass bulbs. When nitrogen is present, a coil of tightly-rolled copper-wire gauze is placed in the front part of the combustion tube and heated to redness, in order to reduce any oxides of nitrogen which may be formed in the subsequent combustion. In the presence of sulphur or of the halogens, lead chromate, which has been

* For details see Sudborough and James' *Practical Organic Chemistry*, Chap. V, B.

fused and then powdered, is used instead of copper oxide, so as to convert any Cl, SO_2, &c., into $PbCl_2$, $PbSO_4$, &c., and thus prevent them from passing into the potash solution. When only halogens, without sulphur, are present, the combustion is carried out with copper oxide, a copper, or still better a silver spiral, which is kept cool, being placed in the fore-part of the tube to retain the halogens.

In the presence of alkalis or alkaline earths (which would retain carbon dioxide), lead chromate mixed with $\frac{1}{10}$ of its weight of potassium bichromate is used; the chromic acid then expels all the carbonic acid.

Explosive compounds must be burnt in a vacuum. From the weights of carbon dioxide and water found, the percentages of C and H are readily calculated:

$$C = \tfrac{3}{11} CO_2;\ H = \tfrac{1}{9} H_2O.$$

Estimation of Nitrogen. This estimation is either relative or absolute In the former case the proportion between the nitrogen and the carbon dioxide evolved is determined (*Liebig, Bunsen*); in the latter the nitrogen is either estimated as such volumetrically, or as ammonia.

The conversion into **Ammonia** is effected by heating the substance strongly with soda-lime (*Will, Varrentrapp*), or by treating it with strong sulphuric acid and permanganate of potash (*Kjeldahl*; Z. Anal. Ch. **22**, 366; also B. **19**, Ref. 852; **24**, 3241; **27**, 1633). The ammonia is then either titrated directly by absorption in standard acid, or transformed into ammonium platinichloride, $(NH_4)_2PtCl_6$, which is weighed, or else ignited, and the weight of the residual metallic platinum noted.

In the **Gasometric Estimation of Nitrogen** the substance is mixed with copper oxide, a copper spiral being also used in the front part of the tube, and the combustion is carried out in the usual way, but in a stream of carbon dioxide; the CO_2 is either generated from magnesite in the tube itself, or led through it. The nitrogen is collected over mercury and aqueous caustic potash (*Dumas*), or directly over potash (*Zulkowsky, Schwarz, Schiff*, &c.), in some special form of nitrometer.

Its percentage is obtained by reducing the volume to the volume at normal temperature and pressure, determining the weight of this volume of nitrogen from the fact that 1 c.c. of

dry nitrogen at 0° and 760 mm. weighs 1·2489 mg., and expressing the result in percentage.

The Gasometric method may be used for all classes of nitrogen compounds, but the Soda-lime method cannot be used for nitro compounds, certain bases, and various other groups of compounds, as the nitrogen of these is not completely transformed into ammonia upon heating with soda-lime.

For the simultaneous determination of carbon, hydrogen, and nitrogen the combustion must be carried on in a stream of pure oxygen, the mixture of gases escaping from the potash bulbs being collected over a solution of chromous chloride, which absorbs the oxygen, but not the nitrogen (A. 1886, **233**, 375).

Estimation of Sulphur and Phosphorus. The **Sulphur** is estimated as sulphuric acid, being converted into this—

(*a*) In the wet way, by heating the substance with fuming nitric acid at 150°–300° in a sealed tube (*Carius*), or in a combustion-tube in a mixed stream of nitric oxide and oxygen (*Claësson*), or nitric acid vapour (*Klason*).

(*b*) In the dry way—(and this method is only available in the case of the less volatile compounds)—by fusing the substance with potassium hydroxide and nitre, or with soda and chlorate or chromate of potash, also by heating with soda and mercuric oxide, or with lime in a stream of oxygen.

Phosphorus is estimated by analogous methods.

Estimation of the Halogens. Here also the organic substance is completely decomposed—

(*a*) After *Carius*, as above, in a sealed tube, with fuming nitric acid and solid silver nitrate, by which means the halogen is converted into its silver salt;

(*b*) By heating the compound strongly with pure lime in a hard glass tube, or in two crucibles, one of which is inverted in the other, or with sodium carbonate and nitre in a tube. The chloride formed is precipitated with silver nitrate in the usual way;

(*c*) By the action of nascent hydrogen (sodium and alcohol), the halogen in the organic substance can frequently be converted into its hydrogen compound (*Stepanow*).

Dennstedt, B. 1897, **30**, 1590, 2861, has described methods for estimating C, H, Cl, and S in one operation.

Metallic and acidic radicals, contained in organic salts, can often be estimated directly by the usual methods.

Oxygen is almost invariably determined by difference; direct

methods of estimation have been proposed by *Baumhauer*, *Ladenburg*, *Stromeyer*, and others.

The carbon estimation is usually too low (0·05 – 0·1), owing to leakage and incomplete absorption, that of hydrogen too high (0·1 – 0·2), owing to the difficulty of completely drying the cupric oxide. Nitrogen estimations are also usually too high, owing to the difficulty of completely freeing the carbon dioxide from air.

The Calculation of the Empirical Formula

The same principle applies here as in the case of inorganic compounds, *i.e.* the percentage numbers found are divided by the atomic weights of the respective elements, the relative proportions of the quotients obtained being expressed in whole numbers. For instance, acetic acid being found to contain 40·11 p.c. carbon, 6·80 p.c. hydrogen, and, consequently, 53·09 p.c. oxygen, the quotients are to each other as 3·34 : 6·80 : 3·32 = 1 : 2 : 1. The simplest analysis-formula of acetic acid would therefore be CH_2O. Sometimes figures are obtained which correspond with equal nearness to different formulæ, between which it is therefore impossible, without further data, to choose.

For instance, a sample of naphthalene yields on analysis 93·70 p.c. carbon and 6·30 p.c. hydrogen; the quotient proportion here is 7·81 to 6·30 = 1·239 : 1, which corresponds equally well with the numbers 5 : 4 or 11 : 9. The formula C_5H_4 requires 93·75 p.c. carbon and 6·25 p.c. hydrogen, and the formula $C_{11}H_9$, 93·62 p.c. carbon and 6·38 p.c. hydrogen, the deviations from the actual numbers found being in both cases within the limits of experimental error. Therefore other considerations must be taken into account here, in order to decide between the two formulæ.

The formula derived from the results of analyses is termed the **Empirical Formula**, and expresses the simplest numerical relationship between the atoms of the elements present. The actual molecular formula may be a multiple of this, and has to be determined according to special principles.

Determination of Molecular Weight

1. By Chemical Methods.

Our chemical formulæ (*e.g.* CH_2O) express not merely

percentage relation, but at the same time the smallest quantity of the compound which is capable of existing as such, *i.e.* a molecule of it. This molecule is ideally no longer divisible by mechanical means, but only by chemical, and then into its constituent atoms. If the formula CH_2O were the correct one for acetic acid, then the amount of oxygen (or carbon) contained in a molecule would be indivisible, and that of hydrogen divisible only by 2. Since, however, it has been observed that one-fourth of the total hydrogen in acetic acid is replaceable, *e.g.* by a metal, with the formation of a salt, it is obvious that the quantity of hydrogen in the molecule must be divisible by 4, and so the formula must contain at least 4 atoms of hydrogen, and must therefore be $C_2H_4O_2$, or some multiple of it. This is, in fact, the case. Acetate of silver contains 64·67 p.c. silver, and therefore 35·33 p.c. of the acetate radical; or, to 1 atom of silver = 108 parts by weight, there are 59 parts by weight of the acid radical. This 59, together with 1 atom of hydrogen = 1, makes the molecular weight of acetic acid 60, = 2 × 30, = 2 × CH_2O, = $C_2H_4O_2$.

This is a determination of molecular weight by chemical means. Such determinations are carried out in the case of acids generally by means of their silver salts; these are usually normal salts, are easy to purify, are almost always free from water of crystallization, and are readily analysed. It is, however, *absolutely necessary* to know whether the acid is mono- or polybasic. In the case of a di-, tri-, &c., basic acid, the above calculation must be made with reference to 2, 3, &c., atoms of silver, whereas acetic acid—being monobasic—contains only one replaceable atom of hydrogen, which is therefore exchanged for one atom of silver. Consequently, its formula cannot be a multiple of $C_2H_4O_2$.

In the determination of the molecular weights of **Bases**, their platinichlorides are similarly made use of, these being almost always constituted on the type of ammonium platinichloride: $(NH_3)_2H_2PtCl_6$: *i.e.* they contain two molecules of a monoacid base such as ammonia combined with one atom of platinum.

To determine the molecular weights of **Neutral Compounds**, derivatives must be prepared and examined for the proportion of the total hydrogen which is replaceable, *e.g.*, by chlorine. For example, by the action of chlorine upon naphthalene, there is first formed the substance monochloronaphthalene, which contains 73·8 per cent C, 4·3 per cent H, and 21·9 per

cent Cl, these numbers giving the formula $C_{10}H_7Cl$. In the same way benzene yields the compound C_6H_5Cl. In both these cases the halogen acts by replacing hydrogen, and at least one atom of the latter in the molecule must be replaced, since fractions of an atom are necessarily out of the question. If, then, the compound obtained has the formula $C_{10}H_7Cl$, it follows that $\frac{1}{8}$th of the H present has been replaced by Cl, and there must consequently be 8, 8×2, or 8×3, &c., atoms of hydrogen in the compound, and likewise 10 atoms, or some multiple of 10, of carbon. But a multiple of 8 or 10 may be rejected, since no compounds have been observed which would indicate the replacement of $\frac{1}{16}$th of the total hydrogen. This leads to the formula $C_{10}H_8$ for naphthalene, the other possible formula got by analysis viz. $C_{11}H_9$ (see p. 7), being now untenable. In a similar way the formula of benzene is found to be C_6H_6.

2. By Physical Methods.

(a) *By Estimating the Vapour Density.*

According to the law of *Avogadro* (1811) and *Ampère* (1814) all gases under similar conditions, *i.e.* in the perfectly gaseous state and under the same temperature and pressure, contain in equal volumes equal numbers of molecules. It follows from this that the weights of equal volumes of different gases are proportional to the weights of equal numbers of their constituent molecules, in other words, the molecular weight is proportional to the specific gravity of the gas. Thus, if M_x be the molecular weight of any given substance required, M_o that of oxygen, S the vapour density or specific gravity of the former as compared with oxygen taken as 16*,

$$M_x : M_o = S : 16.$$

And since $M_o = 32$, $M_x = S \times 2$. To determine, therefore, the molecular weight of a gas or vapour, one has only to find its density, and to multiply this by 2.

To take an example, the specific gravity of acetic acid vapour being found to be 30, then $M = 60$, and the molecular formula is $C_2H_4O_2 = 60$.

* Oxygen is taken as standard ($O = 16$) for vapour density, since it is now customary to take it as standard in atomic-weight determinations. For all practical purposes, one may take the density compared with hydrogen as unity.

solvent produced by the introduction of known weights of the substance into a given weight (or volume) of the solvent. The principles involved are exactly the same as those discussed above in the cryoscopic method, but the forms of apparatus are different. (J. C. S. 1898, **73**, 502.)

Descriptions of apparatus employed in these physical methods are given in Sudborough and James' *Practical Organic Chemistry*, Chap. VIII.

(*c*) *By Measurement of the Osmotic Pressure.*

According to *van't Hoff* (Z. phys. Chem. I. 481), equimolecular solutions exert the same osmotic pressure, or are isotonic, equality of temperature being assumed. From this it follows, by reasoning analogous to that in section (*b*), that the molecular weight of a compound can be ascertained by measuring the osmotic pressure of its solution. The method is rarely used in chemical laboratories. (*Ladenburg*, B. 1889, **22**, 1225; *M. Planck*, Z. phys. Chem., 1890, **6**, 187.)

(*d*) *By Measurement of the Lowering of the Vapour Pressure.*

According to *Raoult*, the same generalizations hold for the lowering of the vapour pressure of a solvent by the introduction of a solute, as for the lowering of the freezing-points or the raising of the boiling-point. Three methods of applying the principle for the determination of molecular weights have been described. This law can be deduced theoretically from the preceding one (*c*), and it also stands in theoretical continuity with that of (*b*). (See *Will & Bredig*, B. 1889, **22**, 1084; *Barger*, J. C. S. 1904, **85**, 206; *Perman*, *ibid.* 1905, **87**, 194; *Blackman*, *ibid.* 1474.)

(*e*) *By Measuring the Decrease in Solubility.*

(*Nernst*, B. **23**, Ref. 619. See also *Ostwald-Luther.*)

Polymerism and Isomerism

The determination of molecular weight is of the first importance, because different substances very frequently have the same percentage composition and therefore the same empirical formula, and yet are totally distinct from one another. This difference is often due to differences in the complexities of the molecules. Thus formic aldehyde, CH_2O; acetic acid, $C_2H_4O_2$; lactic acid, $C_3H_6O_3$; and grape-sugar, $C_6H_{12}O_6$, have all the same percentage composition; as have also ethylene, C_2H_4:

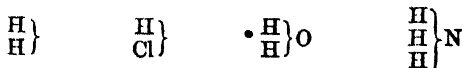
propylene, C_3H_6; and butylene, C_4H_8. Compounds standing in such relation to each other are termed **polymers**. Very frequently, however, substances which are totally distinct from each other possess both the same percentage composition and the same molecular weight; that is to say, these compounds are made up not only of the same elements, but also of an equal number of atoms of these elements; such substances are termed **isomers** or **metamers**. (See Ethers.) Thus, for instance, common alcohol and methyl ether, the latter of which is obtained by heating methyl alcohol with sulphuric acid, have one and the same molecular formula, C_2H_6O.

The striking phenomenon of isomerism is most readily explicable on the assumption that for the molecule of each compound there is a definite arrangement of the atoms, and that this arrangement or grouping is different in the molecules of the two isomerides. This difference in grouping may be considered as being due to a difference in the linking powers of the atoms, as is indicated by the dissimilar chemical behaviour of isomers, and explained by the theory of valency.

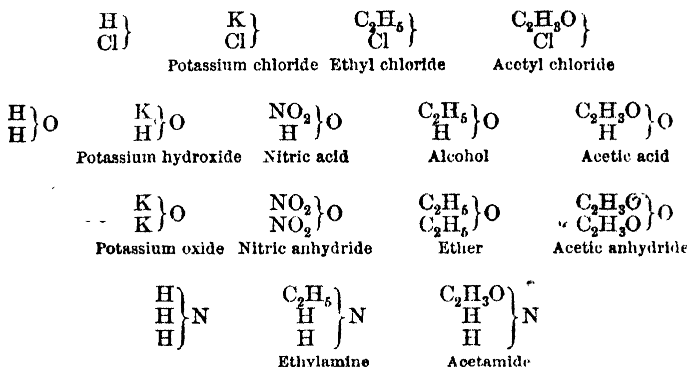
Chemical Theories; the Theory of Valency

After the fall of the Electro-Chemical theory, unitary formulæ—in contradistinction to the earlier dualistic formulæ—were much used; thus alcohol had the formula $C_4H_6O_2$ (using the old equivalent weights). The necessity for comparing substances of complicated composition with simpler ones, taken as "Types", had already repeatedly led to the propounding of new theories for representing the constitution of organic compounds, *e.g.* the older Type theory (*Dumas*), and the Nucleus theory (*Laurent*).

These obtained a firmer basis through *Gerhardt's* Theory of **Types**, which received support more especially from the discovery of ethylamine and other ammonia bases (*Wurtz*, 1849, and *Hofmann*, 1849, 1850), the proper interpretation of the formulæ of the ethers (*Williamson*, 1850), and the discovery of the acid anhydrides (*Gerhardt*, 1851). All compounds, inorganic as well as organic, were in this way compared with simpler inorganic substances taken as "Types", of which *Gerhardt* named four, viz.—



The first two of these really belong to the same type. Thus the following formulæ were arrived at:—



&c. &c. Organic compounds could thus, like inorganic, be referred to inorganic types by assuming in them the presence of Radicals (*e.g.* ethyl, C_2H_5; acetyl, C_2H_3O, &c.), *i.e.* of groups of atoms which play a part analogous to that of an atom of an element, and which can be transferred by double decomposition from one compound to another. Thus ethyl chloride, C_2H_5Cl; alcohol, C_2H_6O; ethylamine, C_2H_7N; ether, $C_4H_{10}O$; &c., were represented as containing the same radical C_2H_5, ethyl, and the close relationship existing between these compounds now found expression in the type formulæ.

Sulphuric acid, H_2SO_4, was derived from the double water type, thus—

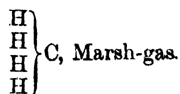


and chloroform, $CHCl_3$, and glycerin, $C_3H_8O_3$, from the triple hydrochloric acid and water types—

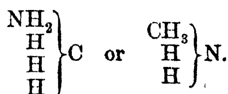


the assumption being made that the radicals $(C_2H_5)'$, $(SO_2)''$, $(CH)'''$, and $(C_3H_5)'''$ could replace a number of hydrogen atoms corresponding with the number of accents (′) marked upon them, *i.e.* that they were monatomic, diatomic, &c. To the above

three types *Kekulé* afterwards added a fourth, of especial importance as regards the carbon compounds, viz.—



It was then found that many compounds could be referred equally well to one or another of these types, methylamine, for instance, either to CH_4 or to NH_3, thus—



The assumption, already mentioned, of the atomic groups (radicals) which in these types replaced hydrogen, led further to more exact investigations of the chemical value, *i.e.* the replaceable value, of those groups as compared with that of hydrogen. In this way chemists learnt to distinguish between mono-, di-, tri-, &c., valent groups, and, generally speaking, to pay more attention to equivalent proportions.

As the outcome of his researches upon organo-metallic compounds, *Frankland* formulated in 1852 (A. **85**, 368) the law that the elements nitrogen, phosphorus, arsenic, and antimony tend to form compounds which contain three or five equivalents of other elements.

Kekulé then, in 1857–58 (A. **104**, 129; **106**, 129), proceeded to show that a more profound idea (the "Type idea") lay at the root of the types themselves, viz., that there are mono-, di-, tri-, and tetravalent, &c., elements, which possess a corresponding replacing or combining value as regards hydrogen; and that hydrogen is therefore monovalent, oxygen divalent, nitrogen trivalent, carbon tetravalent, and so on.

With the introduction of the CH_4 type by *Kekulé*, and the establishment of the tetravalent nature of the carbon atom accompanying this, were connected the endeavours of *Kolbe* to derive the constitution of organic compounds from carbonic acid (according to *Kolbe* C_2O_4, $C = 6$, $O = 8$), by the exchange of oxygen for organic radicals (A. **113**, 293); see also, for further details, *Kopp's* "Entwickelung der Chemie in der neueren Zeit" (Oldenbourg, Munich, 1873), and *E. V. Meyer's*

"History of Chemistry" (Macmillan, 1891), *Schorlemmer's* "Rise and Development of Organic Chemistry" (Macmillan).

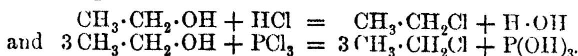
The question of the valency of elements, a point which it is often difficult to decide in inorganic chemistry, is infinitely easier of determination in the case of the carbon compounds, because the carbon atom is tetravalent towards hydrogen as well as towards chlorine and oxygen. Since the atom of hydrogen, as the unit of valency, is monovalent, and, further, since the divalence of the oxygen atom cannot reasonably be doubted, the valency of the three "organic" elements hydrogen, oxygen, and carbon may be considered as resting upon a sure basis, as may also the conclusions drawn therefrom, and this all the more since the most important carbon compounds are made up of those three elements.

Within the past few years the divalency of the oxygen atom in many organic compounds has been brought into question. The readiness with which many oxy-derivatives form definite compounds with mineral acids and with metallic salts would appear to indicate that in many cases the oxygen atom can even be tetravalent (see Oxonium Salts). In certain compounds it has also been suggested that the carbon atom may be di- or trivalent (see Chap. L, E., Carbylamines and Triphenylmethyl).

Explanation of Isomerism; Determination of the Constitution of Organic Compounds

The phenomenon known as isomerism is elucidated to a great extent by the theory of valency. If two substances have the same molecular formula, *i.e.* both contain the same elements and the same number of atoms of the respective elements in their molecules, then the obvious conclusion to be drawn is that in the two molecules the atoms are differently arranged. The methods adopted in determining the manner in which the atoms are linked together, or, as it is called, the determination of the chemical constitution of the compound, is usually based on the following points:—(*a*) The respective valencies of the atoms constituting the molecule. A compound C_2H_6 must have the structural formula $\begin{matrix} H \\ H- \\ H \end{matrix}\!>\!C\cdot C\!<\!\begin{matrix} H \\ -H \\ H \end{matrix}$, or, as it is often more shortly written, $CH_3\cdot CH_3$, if each atom of carbon is to be represented as tetravalent, and each hydrogen atom as monovalent. Similarly the compound CH_4O must be

represented as $\begin{matrix}H\\H\end{matrix}\!>\!C\!<\!\begin{matrix}H\\O-H\end{matrix}$, or $CH_3 \cdot OH$ if the carbon atom is tetravalent, the oxygen atom divalent, and the hydrogen atoms monovalent. (*b*) A study of the more important methods of formation and of the chemical reactions in which the compound in question can take part. To select as an example ethyl alcohol, C_2H_6O. We can start from ethane, $CH_3 \cdot CH_3$, and by the action of chlorine replace one of the hydrogen atoms by a chlorine atom, and thus obtain the compound $CH_3 \cdot CH_2Cl$. When this is boiled with dilute alkalis (KOH), it gives potassium chloride and ethyl alcohol, $C_2H_5Cl + KOH = C_2H_6O + KCl$. From this it is obvious that the monovalent chlorine atom becomes replaced by an atom of oxygen and an atom of hydrogen. This can be readily understood if we assume that these two atoms enter in the form of the monovalent hydroxyl group, —O—H, and the *constitutional formula* for ethyl alcohol would then be $\begin{matrix}H\\H-\\H\end{matrix}\!>\!C-C\!<\!\begin{matrix}H\\H\\O-H\end{matrix}$ or $CH_3 \cdot CH_2 \cdot OH$. This formula is further supported by a study of most of the chemical reactions in which ethyl alcohol can take part. It can react with metallic sodium, yielding a compound, sodium ethoxide, C_2H_5NaO; however much sodium is employed, only one of the six hydrogen atoms present in the alcohol molecule can be replaced by sodium, and this atom is presumably the one differently situated from the remaining five, namely, the one attached to oxygen. The presence of the hydroxyl, —O—H, group is further confirmed by the action of hydrogen chloride or of phosphorus trichloride on the alcohol, when an atom of chlorine takes the place of the ·OH group.

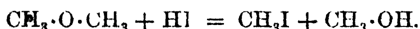


$$CH_3 \cdot CH_2 \cdot OH + HCl = CH_3 \cdot CH_2Cl + H \cdot OH$$

and $$3\,CH_3 \cdot CH_2 \cdot OH + PCl_3 = 3\,CH_3 \cdot CH_2Cl + P(OH)_3.$$

Isomeric with ethyl alcohol is the substance known as dimethyl ether. Although it has the same molecular formula, it differs altogether from ethyl alcohol in its chemical and physical properties. The only other possible method of linking up the atoms 2 C, 6 H, and O, is $\begin{matrix}H\\H-\\H\end{matrix}\!>\!C-O-C\!<\!\begin{matrix}H\\H\\H\end{matrix}$, in which the two carbon atoms are not directly united to one another, and in which the six hydrogen atoms are all similarly

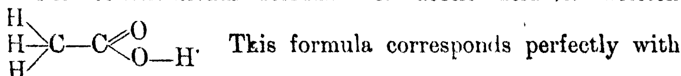
situated. The chemical reactions of dimethyl ether are in perfect harmony with this constitutional formula. It does not react with metallic sodium, and hence presumably does not contain an ·OH group. When acted upon by hydriodic acid, under suitable conditions, the molecule is ruptured, as represented by the following equation:—



$$CH_3{\cdot}O{\cdot}CH_3 + HI = CH_3I + CH_3{\cdot}OH.$$

Similarly, whenever the oxygen atom is removed a rupture of the molecule occurs, and the two carbon atoms in the molecule become separated.

The constitutional formula for acetic acid is written



This formula corresponds perfectly with the chemical behaviour of acetic acid and explains the following facts:—(*a*) that one of the hydrogen atoms of the acid possesses properties different from those of the three others, the first-named being easily replaceable by metallic radicals; (*b*) that the two oxygen atoms behave differently, not being equally readily exchangeable for other radicals; (*c*) that different functions appertain to the two carbon atoms, so that one of them—being already joined to two atoms of oxygen—easily gives rise to carbonic acid, while the other—connected as it is with three atoms of hydrogen—readily passes into methane or methyl compounds.

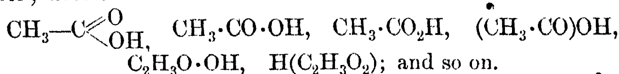
On account of the innumerable cases of isomerism which have been observed, simple molecular formulæ alone are in most cases insufficient for the discrimination of organic compounds; it generally requires the constitutional formulæ to give a clear idea of their behaviour and of their relations to other substances. Careful study has made it possible within the last few decades to find out the mode in which the atoms are combined in the molecules of most organic compounds, and from this to deduce new methods for their preparation. The constitutional formulæ thus arrived at are sometimes simple, sometimes, however, complicated, as, for instance, in the cases of citric acid and grape-sugar (Chaps. XI, B. and XIV, A.).

Rational Formulæ

Great latitude is permissible as regards the mode of writing constitutional formulæ, according to the particular points

which it is desired to emphasize. A formula on paper is not as a rule intended to represent the symmetrical or spatial arrangement of the atoms in a compound.

A shortened constitutional formula, which indicates more chemical relations than an empirical one does, is called a *rational* formula; *e.g.* C_2H_5OH, alcohol; $(CH_3)_2O$, methyl ether; acetic acid.



$$CH_3—C\langle^{O}_{OH},\quad CH_3\cdot CO\cdot OH,\quad CH_3\cdot CO_2H,\quad (CH_3\cdot CO)OH,$$
$$C_2H_3O\cdot OH,\quad H(C_2H_3O_2);\text{ and so on.}$$

A system of shorthand formulæ has been suggested by *Hackh* (Sci., 1918, **48**, 333). The crossing of two lines represents a carbon atom, oxygen and nitrogen atoms are denoted by lines meeting, and hydrogen by lines terminating. Single valencies are denoted by straight and double by curved lines. Acetic acid = ╋ℓ

The Nature of the Carbon Atom

The theoretical views and the knowledge thereby gained of the nature of the carbon atom may be expressed somewhat as follows:—

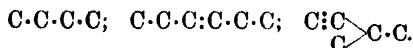
1. The carbon atom is tetravalent.

2. Its four valencies are all equal; a mono-substituted derivative of methane exists in only one form, that is, isomerism is not met with.

3. The atoms or atomic groups which are held bound by these four valencies cannot readily exchange places with each other (the *Le Bel–van't Hoff* law, 1874). Proof: there are in nearly every case two physically different tetra-substitution products, C, a, b, c, d of methane (see Stereochemistry).

4. Several carbon atoms can be connected together by either one, two, or three valencies (see p. 23): C·C, C:C, C⋮C.

5. Similarly, three or more carbon atoms may be united, forming in this way the so-called "carbon chains" (see p. 32), thus—

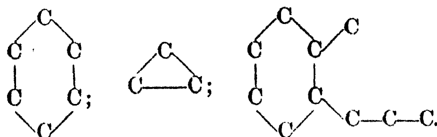


C·C·C·C; C·C·C:C·C·C; C⋮C>C·C (with a further C on the branch)

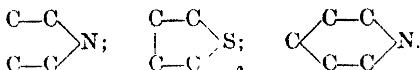
The number of the atoms so linked together may be very large, in some cases probably several hundreds.

6. These carbon atoms form either open or ring-shaped closed chains.

Open chains are those which have separate constituent atoms at either end, as in (5). In *closed chains* or *rings*, on the contrary, the first and last constituent atoms are linked together (although there may at the same time be subsidiary branches from them), thus—



7. The atoms of other elements, with the exception, of course, of monovalent ones, may likewise take part in the formation of such chains, both open and closed; for example:



The above figures (the hexagon, &c.), which are made use of to represent such chains or rings, are merely meant to be pictorial and not geometrical; the question of the spatial arrangement of atoms in compounds is dealt with later. (See Active Valeric Acid, Chap. VI, A.)

Homology

In the study of carbon compounds it is customary to group together all the compounds with similar chemical structure and similar chemical properties, and to arrange the members of such a group, or *homologous series* as it is termed, according to the order of their molecular complexity, *i.e.* according to the number of carbon atoms contained in the molecule.

For example:—

Paraffins.		Fatty acids.
CH_4 methane	......	CH_2O_2 formic
C_2H_6 ethane	......	$C_2H_4O_2$ acetic
C_3H_8 propane	......	$C_3H_6O_2$ propionic
C_4H_{10} butane	......	$C_4H_8O_2$ butyric
&c.		

It is found that in any such *homologous series* a number of generalizations can be drawn. Some of the more important of these are:—

1. For each homologous series we can write a *general for-*

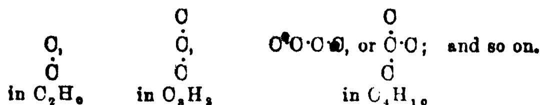
mula which will represent the composition of all the members of the series; for example, the general formula for the paraffins is C_nH_{2n+2}, and for the saturated fatty acids $C_nH_{2n}O_2$.

2. If any particular member in a series is selected, it is found to differ in composition from the member immediately preceding, and also from the one immediately succeeding, it by a definite amount, namely, CH_2. Or, expressed in other words, any member of the series may be regarded as derived from the member immediately preceding it by the introduction of a methyl group, $\cdot CH_3$, for an atom of hydrogen. It follows, therefore, that all the members of the paraffin series may be regarded as derived from CH_4 by the addition of a given number of CH_2 groups, and the general formula is for this series $CH_4 + xCH_2$, or more simply C_nH_{2n+2}.

3. The chemical properties of the different members of the series vary but slightly, so that a description of the chemical properties of any one member may be taken, as a rule, to apply to the other members.

4. In studying the physical properties, well-marked gradations are observed as the number of carbon atoms increases. In the case of liquids, the boiling-point is found to rise as the complexity of the molecule increases. In certain series, *e.g.* the paraffins, the first few members are gases, then follow liquids with gradually increasing boiling-points, and ultimately solids with extremely high boiling-points. Other physical data, such as melting-point, specific gravity, solubility, &c., are affected in very much the same manner.

In the paraffin series the grouping together of the carbon atoms must be conditioned by themselves, since hydrogen, as a monovalent element, cannot be the cause of it. In all the higher hydrocarbons the carbon atoms are therefore combined together in the form of a chain, as shown in the following graphical representations:—



Various cases can occur in the mode of combination of the carbon atoms (Isomers). (See Hydrocarbons of the Methane Series.)

Law of Even Numbers of Atoms.—The number of hydrogen

atoms in the above hydrocarbons is always divisible by two. Should they therefore be partially replaced by other elements, the sum of these latter, if their valencies are expressed by odd numbers, *e.g.* Cl, N, and P, and of the remaining hydrogen atoms taken together must, as a necessary consequence of the law of equivalent proportions, remain an even number.

Radicals

According to *Liebig*, radicals were groups of atoms capable of a separate existence, which played the parts of elements, and, like these latter, could combine among themselves and be exchanged from one compound to another.

Later on, the postulate that such radicals must also be capable of existing in the free state was allowed to lapse, and they were frequently defined shortly as "the residues left unattacked by certain decompositions".

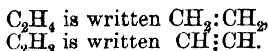
Now, however, it is usual to designate as radicals only those atomic groups which are found repeating themselves in a comparatively large number of compounds derived from one another, and which play in these compounds the part of a simple element, *e.g.* CH_3, methyl; C_2H_3O, acetyl; by this definition the question of their existence or non-existence in the free state does not arise. The radical methyl, for example, is not known in the free state, since, when its formation might be expected, ethane (dimethyl), $CH_3—CH_3$, is obtained instead (see p. 37). Such radicals may be mono-, di-, or trivalent, &c., according to the number of monovalent atoms which they are capable either of replacing or of combining with, so as to form a saturated compound; for instance, $(C_2H_4)''$, ethylene, is divalent; $(C_3H_5)'''$, glyceryl, trivalent; $(CH)'''$, methine or methenyl, likewise trivalent, &c. The monovalent residues, C_nH_{2n+1} (methyl, ethyl, &c.), which form the radicals of the monovalent alcohols, $C_nH_{2n+1}OH$, are frequently termed *alkyls*, or *alphyls*, while the divalent residues, C_nH_{2n}, are known as *alkylenes*.

At the present time it is also customary to speak of single atoms as radicals; *e.g.* we have the chloride or iodide radical, and further, the hydric radical which is characteristic of acids.

Classification of the Hydrocarbons, &c.

The hydrocarbons which have already been described are termed "saturated" compounds, since they cannot take up more hydrogen. But besides these there are hydrocarbons, &c., poorer in hydrogen, or "unsaturated", such as C_2H_4, ethylene, and C_2H_2, acetylene, corresponding with which there are numerous homologous series.

The constitution of these is explained, as will be seen later, by the assumption of a double or triple bond between neighbouring carbon atoms, for instance—


C_2H_4 is written $CH_2:CH_2$,
C_2H_2 is written $CH\vdots CH$.

From these different hydrocarbons, as starting-points, the most various substitution products, such as alcohols, aldehydes, ketones, acids, amines, &c., are derived by exchange of the hydrogen for halogen, oxygen, nitrogen, &c.

To another class of hydrocarbons belongs that most important compound benzene, C_6H_6, which contains eight atoms of hydrogen less than hexane, C_6H_{14}. With regard to its constitution, the theory of the existence of a closed chain of six carbon atoms has been advanced. (See Benzene Derivatives.) From benzene are derived an immense number of the most different homologous and analogous hydrocarbons and substitution products, alcohols, aldehydes, acids, and so on. Thus benzene, like methane, is the mother substance of numerous organic compounds.

What has just been said with regard to benzene also holds good for various other compounds, which are characterized from a chemical point of view by containing a closed (ring) chain. These are:—

(*a*) Trimethylene, C_3H_6; Tetramethylene, C_4H_8; and Pentamethylene, C_5H_{10}.

(*b*) Pyridine, C_5H_5N, a strongly basic nitrogenous compound, but one which at the same time resembles benzene closely in many respects.

(*c*) Furane, C_4H_4O; Pyrrol, C_4H_5N; Thiophene, C_4H_4S; Pyrazole, $C_3H_4N_2$; Thiazole, C_3H_3NS; &c.

Some of these latter compounds are extremely like benzene, others like pyridine; several of them are as yet only known in the form of derivatives. Like benzene, they are all mother substances of—in many cases—long series of compounds.

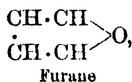
Organic chemistry is therefore divided into the following sections:—

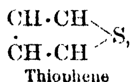
1. **Chemistry of the Methane Derivatives or Fatty Compounds, or Aliphatic Compounds** (from ἀλοιφή, fat), so called because the fats and many of their derivatives belong to this group. This section comprises all carbon compounds with open chains. A few compounds, which are really closed-chain or ring compounds, will be mentioned in this section on account of their close relationship to certain open-chain compounds; as an example, we may take succinic anhydride $\begin{matrix} CH_2\cdot CO \\ CH_2\cdot CO \end{matrix}\!\!>\!O$, which is formed by the elimination of water from succinic acid, $OH\cdot CO\cdot CH_2\cdot CH_2\cdot CO\cdot OH$.

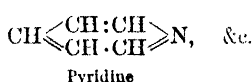
2. **Cyclic or closed-chain compounds.** This section is usually divided into two sub-sections.

(*a*) Chemistry of the *carbocyclic compounds*, which comprises the study of all compounds built up of a ring of carbon atoms. As examples we have $\begin{matrix} CH_2 \\ CH_2 \end{matrix}\!\!>\!CH_2$, Trimethylene; $CH_2\!<\!\begin{matrix} CH_2 \\ CH_2 \end{matrix}\!>\!CH\cdot CO_2H$, Tetramethylene carboxylic acid; $CH\!\lessgtr\!\begin{matrix} CH:CH \\ CH\cdot CH \end{matrix}\!\gtrless\!CH$, Benzene; &c.

(*b*) Chemistry of the *heterocyclic compounds*, comprising the study of all ring compounds which contain other atoms, in addition to carbon atoms, as part of the ring, *e.g.*


Furane


Thiophene


Pyridine

&c.

Physical Properties of Organic Compounds

The physical properties of organic compounds are often of the greatest importance for their characterization, and physical data are frequently made use of in determining the purity of a chemical compound.

Solubility. — The carbon compounds vary enormously as regards their solubility in various solvents. As a rule, a given solvent dissolves those substances which are chemically closely allied to it. As example of this, we have the fact that water tends to dissolve hydroxylic compounds, especially if

there are several hydroxy groups in the molecule, *e.g.* mannitol, glucose, and pyrogallol.

Benzene tends to dissolve most hydrocarbons, and ether dissolves the majority of simple organic compounds, with the exception of salts of acids.

The usual method of determining the solubility of the given substance is to prepare a saturated solution of the substance at the temperature required. This is accomplished by one of two methods:—(*a*) Shaking the finely-divided solute for some time in contact with the solvent at the given temperature, care being taken that there is always some undissolved solute left over. (*b*) If the solute is more soluble in hot than in the cold solvent, a concentrated hot solution is prepared, and is then allowed to cool down to the temperature required, care being taken to stir the solution so that the excess of solute crystallizes out and a supersaturated solution is not obtained. A known weight or volume of the clear saturated solution is taken, and the solvent removed by evaporation, and the residual solute weighed. The result is usually expressed in the form 100 grams of solvent dissolve x grams of solute at t°.

Specific Gravity and Specific Volume.—The specific gravity of a liquid is an important criterion for the purity of the substance. This is usually determined in a specific-gravity bottle, Sprengel tube, or Pyknometer. The pyknometer is filled with pure water at a given temperature (usually 4° or 15°) and carefully weighed. It is then dried, filled with the liquid at a fixed temperature, and again weighed. The ratio $\frac{\text{wt. of liquid}}{\text{wt. of water}}$ is the specific gravity. It is usual in giving the specific gravity to denote the temperature at which the determination was made, as this varies with the temperature, and also the temperature of the water, *e.g.* $d\frac{20^\circ}{4^\circ}$ denotes the specific gravity of the liquid at 20° compared with that of water at 4°. The reciprocal of the specific gravity is known as the *specific volume*, and the product of this and the molecular weight as the *molecular volume.*

Melting-Point.—Each fusible compound has a fixed definite melting-point, and this constant is often made use of in determining the purity of a solid, as the introduction of even small amounts of impurities lowers the melting-point considerably. When appreciable amounts of impurities are present, the

melting-point is not sharp, but ranges over a number of degrees. The melting-point is best defined as the temperature at which the liquid and solid phases of the compound are in equilibrium. The most direct and most accurate method of determining the melting-point is to place a thermometer in the molten substance and allow it to partially solidify, and note the temperature at which the mercury remains constant when the mixed solid and liquid is stirred by the thermometer. As this method involves the use of a relatively large amount of the substance, the determination is usually made by introducing a very small amount of the finely-divided substance into a narrow capillary tube closed at one end. This tube is then attached to a thermometer, the substance being at the same level as the middle of the bulb of the thermometer, and the two are carefully heated in a bath of sulphuric acid. Just before the melting-point is reached the flame is removed occasionally, so that the temperature rises very slowly, and the melting-point can be read accurately to within ·5 or ·25 of a degree. As a rule, a short thermometer is used, so that the whole thread of mercury is in the bath, otherwise a correction has to be made for the length of the mercury thread which is not immersed in the hot bath.

Boiling-Point.—The purity of a volatile substance can usually be determined by means of the boiling-point, *i.e.* the temperature at which the vapour pressure of the substance is equal to the atmospheric pressure. It is usually determined by placing the bulb of the thermometer in the vapour, and if a short thermometer is employed, and the whole of the mercury thread is surrounded by the vapour, no correction is required. In each case the barometric pressure should be stated, and also whether the thread of mercury was completely immersed in the vapour.

Many substances which decompose when heated under atmospheric pressure, may be distilled without undergoing decomposition under reduced pressure. This is accomplished by attaching the flask, condenser, and receiver to a mercury or water pump and exhausting. When the pressure is sufficiently reduced the substance is distilled, care being taken that the pressure under which the distillation occurs is measured by means of a manometer. As a rule, considerable difficulty in avoiding bumping is encountered in distillations under diminished pressure; this is most readily got over by placing a piece of porous material (unglazed pot) in the liquid,

or by slowly aspirating bubbles of air through the boiling liquid. (Compare *Auschütz* and *Reilter*, Brochure. Bonn, 1895).

Fractional Distillation.—Two miscible liquids with widely differing boiling-points, *e.g.* alcohol, 78°, and aniline, 185°, can be separated by the process of fractional distillation, as the lower boiling liquid distils over first. In all cases an intermediate fraction consisting of a mixture of the substances is obtained, but, as a rule, the greater the difference between the boiling-points of the two substances the smaller is this fraction. In many cases where the boiling-points are not very far removed, *e.g.* benzene, 80°, and toluene, 111°, the two compounds cannot be separated by a single fractionation; it is thus customary to collect fractions every 5° and to subject each of these fractions to further distillation, using the same flask for distillation, and again collecting every 5°. It is then found that there is a large fraction boiling at 80–85° and consisting of nearly pure benzene, and a large fraction, 110–111°, consisting of pure toluene, and a number of small fractions boiling at 85–90°, 90–95°, &c., and consisting of mixtures of benzene and toluene. The process is often quickened by using some form of fractionating column. This consists of a long tube with bulbs blown on, and serves to lengthen the neck of the flask. The Linneman tube contains small wire-gauze cups in the constricted parts, and in these drops of the higher boiling liquid collect, and thus all the vapour has to pass through or be washed by these drops. The same purpose is served in the Glynsky tube by placing a glass ball in each constriction. (See *S. Young*, "Fractional Distillation". London, 1903.)

It is not always possible to separate liquids by fractional distillation, for example, when the boiling-points are very close, or when the two substances form a mixture of definite boiling-point. When dilute nitric acid is distilled, water first passes over, and then a mixture of water and nitric acid, until the residue in the flask is 68 per cent nitric acid, and then it boils constantly at 126°, since the vapour and the liquid in the flask have the same composition.

Mixtures of constant boiling-point are always characterized by the fact that they have a vapour pressure either higher or lower than that of either of the constituents, or than that of any other mixture of the same compounds.

Steam Distillation.—This is the process frequently resorted to in the separation of a compound readily volatile in steam

from other substances, *e.g.* tars or inorganic salts, which are not volatile. It consists in blowing steam through the mixture, and condensing the steam and volatile compound by means of a Liebig condenser. Very often the volatile compound is practically insoluble in water, and separates as an oil or solid in the distillate. The rapidity with which a given substance distils with steam depends on the vapour pressure of the substance at the given temperature, and also on its molecular weight or vapour density compared with that of water. Thus a mixture of nitro-benzene and water, which may be regarded as non-miscible liquids, boils at 99°; *i.e.* the vapour pressure of the mixture at 99° is 760 mm. The vapour pressure of water at 99° is 733 mm., and therefore the partial pressure of the nitro-benzene is 27 mm. In a given volume of the mixed vapours $\frac{733}{760}$ will consist of steam and $\frac{27}{760}$ of nitro-benzene, and the relative weights of these volumes will be the volumes × relative densities, *i.e.* $\frac{9 \times 733}{760} : \frac{61 \times 27}{760}$ *i.e.* 4 : 1; or, in other words, $\frac{1}{5}$th by weight of the total distillate will consist of nitro-benzene.

Other methods very frequently used in the purification of solid compounds are crystallization and fractional crystallization. The method employed is essentially the same as that made use of in purifying inorganic compounds, except that organic solvents, *e.g.* alcohol, chloroform, benzene, carbon disulphide, and low-boiling petroleums, are largely used. Often a mixture of two solvents is more serviceable than a single one, *e.g.* substances are often crystallized by solution in warm alcohol and addition of water, or solution in benzene and addition of light petroleum, until a turbidity ensues. The fact that a substance crystallizes from a given solvent in well-defined crystals does not necessarily indicate that the substance is a single chemical individual, as numerous examples of mixed crystals with definite melting-points are known, and these are not resolved when repeatedly crystallized from the same solvent.

Extraction with Ether, Benzene, &c.—Partition Coefficient.—An organic compound can often be separated from other substances, especially inorganic salts, by shaking out with ether, separating the ethereal layer by means of a separating funnel, drying the solution with granular calcium chloride or some other suitable drying agent, and removing the ether by

distillation. The method gives very good results when the compound to be extracted is much more soluble in ether than in water, and when the substances from which it is to be separated are insoluble in ether. When there is no marked difference in the solubilities of the given compound in ether and in water, the extraction must be repeated a number of times, in some cases even twenty, since for each compound the ratio $\frac{\text{conc. of ethereal solution}}{\text{conc. of aqueous solution}}$ is a constant, and is usually termed the *partition coefficient* or *coefficient of distribution* of the particular substance between the two solvents. In extractions with ether it must be borne in mind that ether dissolves to an appreciable extent in water, and also water in ether. Other liquids, such as benzene, carbon-disulphide, chloroform, &c., may be used in place of ether.

When the amount of solvent to be used is limited, it is more economical to extract two or three times with small amounts of solvent rather than only once with the whole amount. As an illustration. 11 grams of a substance and 1 litre each of the non-miscible liquids, water and benzene. The solubility of the substance in benzene is ten times its solubility in water, and it has the same molecular weight in both solvents.

Case I.—Extracting at once with the litre of benzene, $\frac{\text{conc. of benzene solution}}{\text{conc. of water solution}} = \frac{10}{1}$, *i.e.* $\frac{1}{11}$th of the whole, or 1 gram, remains in the water.

Case II.—Extract twice with 500 c.c. of benzene. After first extraction, suppose x grams passes into the benzene, then conc. of aqueous solution is $11 - x$, and of the benzene $2x$, $\therefore \frac{2x}{11 - x} = \frac{10}{1}$, or $x = 9$ (approx.), and 2 grams are left in the water.

After extraction with second quantity of benzene, y grams go into the benzene. Then $\frac{2y}{2 - y} = \frac{10}{1}$, or $y = 1{\cdot}7$ (approx.), and only 0·3 gram remains in the aqueous solution. Whereas, after the single extraction with a litre of benzene 1 gram was left.

For applications of this method in determining the relative strengths of acids and amines, compare *Farmer* and *Warth* (J. C. S. 1904, 1713).

Class I.—ALIPHATIC OR OPEN-CHAIN COMPOUNDS

I. HYDROCARBONS

A. Saturated Hydrocarbons, C_nH_{2n+2}

This constitutes the simplest homologous series of carbon compounds, and all the saturated open-chain compounds may be regarded as derived from these.

The following list includes the more important *normal* hydrocarbons:—

Formula.	Name.	Melting-point.	Boiling-point.	Specific gravity.
CH_4	Methane	−186°	−160°	0·415 at b.-p.
C_2H_6	Ethane	−172	−93	0·446 at 0°
C_3H_8	Propane		−45°	0·536 at 0°
C_4H_{10}	Butane		+1	0·600 at 0°
C_5H_{12}	Pentane		36·3°	0·627 at 14°
C_6H_{14}	Hexane		69°	0·658 at 20°
C_7H_{16}	Heptane		98	0·683 at 20°
C_8H_{18}	Octane		125·8°	0·702 at 20°
C_9H_{20}	Nonane	−51°	150	0·718 at 20°
$C_{10}H_{22}$	Decane	−31°	173°	0·730 at 20°
$C_{11}H_{24}$	Undecane	−26°	195°	0·774 at m.-p.
$C_{12}H_{26}$	Dodecane	−12°	214	0·773 at m.-p.
$C_{14}H_{30}$	Tetradecane	+4°	252°	0·775 at m.-p.
$C_{16}H_{34}$	Hexadecane	18°	287°	0·775 at m.-p.
$C_{20}H_{42}$	Eicosane	37°	205°*	0·778 at m.-p.
$C_{21}H_{44}$	Heneicosane	40°	215°*	0·778 at m.-p.
$C_{23}H_{48}$	Tricosane	48°	234°*	0·779 at m.-p.
$C_{31}H_{64}$	Hentriacontane	68°	302°*	0·781 at m.-p.
$C_{35}H_{72}$	Pentatriacontane	75°	331°*	0·782 at m.-p.
$C_{60}H_{122}$	Hexacontane	101°		

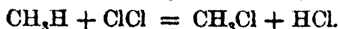
* Under 15 mm. pressure.

The first members of the series, including those with about four atoms of carbon, are gases, which gradually become more easily condensable as the number of carbon atoms in the molecule increases. The members which follow are liquid at the

ordinary temperature, their boiling-point rising with increasing number of carbon atoms. An increase of CH_2 in the molecular formula does not necessarily denote a definite increase in the boiling-point. The difference in boiling-point between hexane and heptane is 29°, and between undecane and dodecane only 19°; thus with compounds of high molecular weight an increase of CH_2 does not produce so marked an effect on the boiling-point as with simpler compounds. The higher homologues, from about $C_{16}H_{34}$ (melting-point 18°) on, are solid at the ordinary temperature, and their melting-point gradually rises up to about 100°. The highest members can be distilled under diminished pressure only. The methane homologues are almost or quite insoluble in water; alcohol dissolves the gaseous members to a slight extent, the liquid members easily, and the solid with gradually increasing difficulty. Their specific gravities at the melting-point increase with increasing number of carbon atoms from 0·4 up to 0·78, which is the maximum limit. This value is already almost reached by the hydrocarbon $C_{11}H_{24}$, so that for the higher members of the series the following law holds good: "the molecular volumes are proportional to the molecular weights" (*Krafft*).

They are incapable of combining further with hydrogen or halogens (see p. 23), and absorb neither bromine nor sulphuric acid. They are therefore termed the Saturated Hydrocarbons. Even fuming nitric acid has little or no action upon the lower members of the series; thus, methane is not attacked by a mixture of fuming nitric and sulphuric acids, even at 150°. They are also very indifferent towards chromic acid and permanganate of potash in the cold,* when oxidation does take place, they are mostly converted directly into carbonic acid. The name of "The Paraffins" (from *parum affinis*), which was originally applied only to the solid hydrocarbons from lignite, has therefore been extended to the whole homologous series.

By the action of the halogens (Cl, Br), **substitution** takes place, the substituted hydrogen combining with an amount of halogen equal to that which has entered the hydrocarbon (see Substitution products of the Hydrocarbons):



$$CH_3H + ClCl = CH_3Cl + HCl.$$

As the number of carbon atoms increases, the percentage composition of these hydrocarbons approaches a definite limit,

* With the exception of compounds containing the grouping R'R''R'''CH.

viz. that of the hydrocarbons, C_nH_{2n}, or CH_2, as is shown by the following table:—

Per cent.	CH_4	C_2H_6	C_3H_8	C_6H_{14}	$C_{16}H_{34}$	$C_{22}H_{46}$	$C_{24}H_{50}$	$C_{35}H_{72}$	Limit Value, C_nH_{2n}
C	75·00	80·00	81·82	83·72	84·60	85·16	85·21	85·36	85·71
H	25·00	20·00	18·18	16·28	15·40	14·84	14·79	14·64	14·29

'It is therefore impossible to distinguish by elementary analysis between two of the neighbouring higher homologues, *e.g.* C_{22} and C_{24}, C_{24} and C_{30}; the only reliable data here are the methods of formation from compounds in which the number of carbon atoms in the molecule is already known, and the melting-points.

Isomers.—Only one representative each of the formulæ CH_4, C_2H_6, and C_3H_8 is known, but of C_4H_{10} there are two, of C_5H_{12} three, and of C_6H_{14} already five isomers, and most of the higher hydrocarbons are known in various isomeric forms. From this the conclusion is drawn that in these different isomers the carbon atoms are differently combined, in the one case in a straight line without branching, like the links of a chain; in the other, with the formation of a branching chain. (This is of course not to be taken as meaning that they are grouped together in space in straight lines.) Thus:—



The first of these hydrocarbons, with a non-branching chain, are termed the normal hydrocarbons; the last, the iso-hydrocarbons.

The principles by which such constitutional formulæ are arrived at will be explained under Butane and Pentane.

Only those homologues are comparable whose constitutions are similar, as in the case of the normal hydrocarbons.

Occurrence.—The hydrocarbons of the paraffin series occur naturally in great variety. Thus, methane is exhaled from the earth's crust, as "fire-damp" and as marsh-gas. The next higher homologues are found dissolved in petroleum, which also contains the higher hydrocarbons in large amount. Solid hydrocarbons occur as ozokerite or earth-wax. By the fractional distillation of petroleum a large number of these com-

pounds have been isolated. Heptane and hexadecane are also found in the vegetable kingdom.

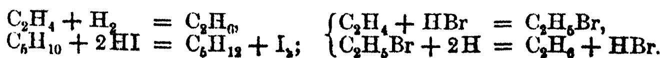
Modes of formation.—A. Various members of this series are obtained by the distillation of lignite (Boghead, Cannel coal), wood, bituminous shale, and, in very much smaller quantity, from pit coal. Paraffins are also obtained by dissolving carbide of iron in acids, and by heating wood, lignite, and coal, but not graphite, with hydriodic acid.

B. From substances containing an equal number of carbon atoms in the molecule.

1. From the alkyl halides,* $C_nH_{2n+1}X$, and, generally speaking, from the substitution products of the hydrocarbons by exchange of the halogen for hydrogen (inverse substitution). This is effected by the action of reducing agents, that is, agents which give rise to nascent hydrogen. Some of the commoner reducing agents employed for such purposes are sodium amalgam and water, zinc and a dilute acid, zinc and water at 160°, the copper-zinc couple in presence of water and alcohol (*Gladstone-Tribe*), aluminium- or magnesium-amalgam and alcohol, and one of the most vigorous reducing agents, concentrated hydriodic acid at high temperatures, especially in contact with red phosphorus, which serves to continually renew the hydrogen iodide. (See Chap. XLIV, Reduction.)

2. From monohydric alcohols, $C_nH_{2n+1}\cdot OH$, polyhydric alcohols, $C_nH_{2n}(OH)_2$, $C_nH_{2n-1}(OH)_3$, &c., also from aldehydes, $C_nH_{2n+1}\cdot CHO$, ketones, $C_nH_{2n+1}\cdot CO\cdot C_nH_{2n+1}$, and other compounds containing oxygen, by heating with hydriodic acid and red phosphorus at relatively high temperatures. In all these reactions the oxygen is ultimately removed as water.

3. From hydrocarbons poorer in hydrogen, *i.e.* unsaturated hydrocarbons (see these), by the addition of hydrogen; *e.g.* ethane from ethylene or acetylene and hydrogen, either in presence of platinum black or finely-divided nickel or by heating the mixture of gases to 400°–500°. Also by heating with hydriodic acid (*Krafft*), or by addition of halogen or halogen hydride, and exchange of the halogen for hydrogen, according to 1. Thus:—



$$C_2H_4 + H_2 = C_2H_6, \qquad \begin{cases} C_2H_4 + HBr = C_2H_5Br, \\ C_2H_5Br + 2H = C_2H_6 + HBr. \end{cases}$$
$$C_6H_{10} + 2HI = C_6H_{12} + I_2;$$

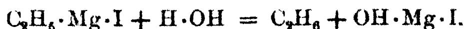
* The monovalent residues, C_nH_{2n+1}, methyl, ethyl, &c., which are at the same time the radicals of the monohydric alcohols, $C_nH_{2n+1}OH$, are frequently termed alkyl groups.

4. By decomposing the organo-zinc compounds (zinc-alkyls), with water (*Frankland*)—



$$Zn(C_2H_5)_2 + 2\,H_2O = Zn(OH)_2 + 2\,C_2H_6.$$

Or more readily by decomposing Grignard's organo-magnesium compounds with water. Thus ethyl iodide and magnesium, in presence of dry ether, yield ethyl magnesium iodide, $C_2H_5 \cdot Mg \cdot I$, and this with water evolves ethane:



$$C_2H_5 \cdot Mg \cdot I + H \cdot OH = C_2H_6 + OH \cdot Mg \cdot I.$$

C. From acids containing more carbon, with separation of carbon dioxide. Thus, by heating acetate of calcium with soda-lime, methane and carbonic acid are formed:

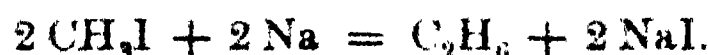


$$(CH_3COO)_2Ca + Ca(OH)_2 = 2\,CH_4 + 2\,CaCO_3.$$

In the case of the acids of higher molecular weight, this separation of carbonic acid is conveniently effected by heating with sodium ethoxide.

D. By the combination of two radicals containing a smaller number of carbon atoms.

1. By the action of sodium upon the alkyl iodides in ethereal solution (*Wurtz*); or by heating with zinc in a sealed tube (*Frankland*):



$$2\,CH_3I + 2\,Na = C_2H_6 + 2\,NaI.$$

By this method also two different radicals can be combined, *e.g.* $C_2H_5I + C_4H_9I$ give $C_2H_5 + C_4H_9 = C_6H_{14}$, ethyl-butyl (*Wurtz's* "Mixed Radicals").

2. By the electrolysis of solutions of the potassium salts of fatty acids (*Kolbe*, 1848). The anions, for example, $CH_3 \cdot COO$, when discharged at the anode, break up into CH_3 and CO_2 and two of the CH_3 groups immediately combine to form a molecule, $CH_3 \cdot CH_3$, viz. ethane. The hydrogen is here evolved at the cathode, and the hydrocarbon at the anode; the carbon dioxide is to a large extent retained in the solution.

Methane, CH_4 (*Volta*, 1778). *Occurrence.*—As an exhalation from the earth's crust, more especially at Baku in the neighbourhood of the Caspian Sea (the "Holy Fire" of Baku); from the large gas wells at Pittsburg, in North America, and in numerous other places; in the exhalations from mud volcanoes, for instance at Bulganak in the Crimea, where the gas is almost pure methane (*Bunsen*); and as pit gas or "fire-damp" in mines, where, when mixed with air, it is apt to cause explosions.

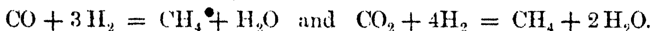
As marsh-gas, together with carbon dioxide and nitrogen,

by the decomposition of organic substances under water; further, by the fermentation of cellulose, *e.g.* by river mud, by means of Schizomycetes (fission-fungi). It is also found in rock-salt (the Knistersalz of Wieliczka), and in the human intestinal gases (up to 57 per cent CH_4 after eating pulse).

The illuminating gas obtained by the destructive distillation of coal contains about 40 per cent methane.

Modes of preparation.—1. Methane is formed synthetically by the direct union of carbon and hydrogen. Pure sugar carbon freed from all traces of hydrogen by treatment with chlorine is heated in a current of dry hydrogen in a porcelain tube, and the issuing gas is found to contain 1 per cent of methane (*Bone* and *Jerdan*, J. C. S., 1897, 41; 1901, 1042; *Pring*, 1910, 489; *Pring* and *Fairlie*, 1911, 1796; 1912, 91); and is also formed by the decomposition of ethane, ethylene, and acetylene at moderate temperatures (*Bone* and *Coward*, 1908, 1197).

2. By the catalytic reduction of carbon monoxide or dioxide by hydrogen in the presence of reduced nickel at 200–250° (*Sabatier* and *Senderens*):



$$CO + 3H_2 = CH_4 + H_2O \quad \text{and} \quad CO_2 + 4H_2 = CH_4 + 2H_2O.$$

3. By leading sulphuretted hydrogen and carbon bisulphide vapour over red-hot copper (*Berthelot*); $CS_2 + 2H_2S + 8Cu = CH_4 + 4Cu_2S$.

4. By passing carbon monoxide and steam over certain heated metals or metallic oxides (*Vignon*, C. R., 1913, **157**, 131).

5. It is usually prepared by heating anhydrous sodic acetate with baryta, or even with soda-lime (p. 34); by-products are ethylene, C_2H_4, and hydrogen (up to 8 per cent).

6. Another method is from aluminium carbide and water, and removing the acetylene and hydrogen (J. C. S., 1913, **103**, 1292).

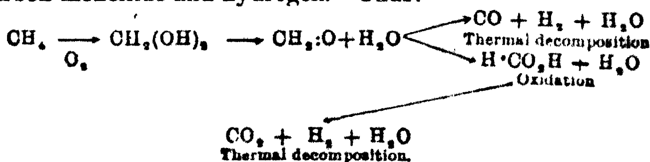
7. Pure methane is obtained from magnesium methyl iodide and water, $CH_3 \cdot Mg \cdot I + H \cdot OH = CH_4 + OH \cdot Mg \cdot I$; also (see B. 1) by the reduction of methyl iodide, CH_3I, *e.g.* in alcoholic solution by means of zinc in the presence of precipitated copper (the *Gladstone-Tribe* "Copper-zinc Couple"); also by the inverse substitution of $CHCl_3$, or CCl_4.

Properties (for summary, see J. ph. Chem., 1918, **22**, 529).—It is a gas with a density = 8 (H = 1), and is condensed under a pressure of 140 atmospheres at 0°. It boils at −164°, and solidifies at −186°. Absorption coefficient in cold water about 0·05, in cold alcohol 0·5. It burns with a

pale and only faintly luminous flame, yielding carbon dioxide and water, and when mixed with air or oxygen in certain proportions forms an explosive mixture. It is decomposed by the electric spark into its elements, and a similar decomposition occurs when the gas is led through a red-hot tube; but there are formed at the same time C_2H_6, C_2H_4, C_2H_2, and, in smaller quantity, C_6H_6, benzene, $C_{10}H_8$, naphthalene, and other products. The first three hydrocarbons just mentioned, ethane, &c., behave similarly.

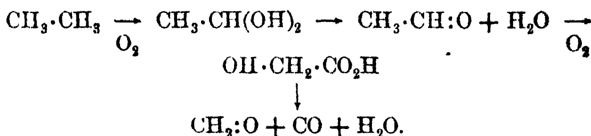
Combustion of Hydrocarbons.—When methane and hydrocarbons generally are burnt or exploded with excess of air or oxygen, the final products are carbon dioxide and water vapour, and the reaction is generally represented, *e.g.*, by the equation $CH_4 + 2\,O_2 = CO_2 + 2\,H_2O$. This undoubtedly represents the final products which are formed, and also their relative amounts, but does not give an idea of the mechanism of combustion. Numerous investigators have conducted experiments on combustion, especially on combustion in the presence of limited amounts of oxygen. The conclusion was first drawn that with a defective supply of oxygen the hydrogen is oxidized in preference to the carbon. Somewhat later, *Kersten* (1861) suggested the preferential burning of the carbon, since when ethylene is exploded with its own volume of oxygen, carbon monoxide and hydrogen are the chief products. (Cf *Smithells*, J. C. S. 1892, **61**, 220.)

The recent work of *Bone* and others on the slow combustion of methane, ethane, ethylene, and acetylene (J. C. S. 1902, 535; 1903, 1074; 1904, 693, 1637; Proc. 1905, 220; B. A. Report, 1910, 469), shows that by passing a mixture of methane and oxygen in a continuous stream through a tube filled with porous material (pot or magnesia), at a fixed temperature between 350° and 500°, appreciable amounts of formaldehyde are obtained. Gaseous products are also obtained, but these are probably due to secondary reactions, *e.g.* either the further oxidation of the aldehyde to carbon monoxide, carbon dioxide and steam, or the thermal decomposition of the aldehyde into carbon monoxide and hydrogen. Thus:—



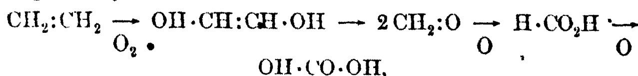
By the expression thermal decomposition is meant that at the temperature mentioned the aldehyde is unstable, and immediately decomposes into the simpler products, CO and H_2.

Ethane behaves similarly, and the reactions can be represented by the following scheme:—



$$CH_3{\cdot}CH_3 \xrightarrow[O_2]{} CH_3{\cdot}CH(OH)_2 \rightarrow CH_3{\cdot}CH{:}O + H_2O \xrightarrow[O_2]{} OH{\cdot}CH_2{\cdot}CO_2H \downarrow CH_2{:}O + CO + H_2O.$$

Secondary reactions are the thermal decompositions of the formaldehyde into CO and H_2, and of the acetaldehyde into CH_4 and CO. In reality some 80 per cent of the ethane can be collected as formaldehyde. With ethylene the reactions are probably—



$$CH_2{:}CH_2 \xrightarrow[O_2]{} OH{\cdot}CH{:}CH{\cdot}OH \rightarrow 2\,CH_2{:}O \xrightarrow[O]{} H{\cdot}CO_2H \xrightarrow[O]{} OH{\cdot}CO{\cdot}OH,$$

and the thermal decomposition products of the formaldehyde, formic acid, and carbonic acid, viz. H_2, CO, CO_2, H_2O.

It is thus obvious that at the temperatures mentioned (350–500°) combustion consists primarily in the addition of oxygen and the production of hydroxylic compounds, which then yield aldehydes. It is highly probable that reactions of a similar nature occur during explosive combination and detonation at high temperatures (B. A. Report, 1910, 492).

Ethane, C_2H_6, occurs in crude petroleum and constitutes the gas of the Delamater gas well in Pittsburg, and is there utilized for technical purposes.

Preparation.—By the electrolysis of acetic acid (*Kolbe*, 1848), and therefore formerly called "methyl" since it was supposed to be CH_3; subsequent molecular-weight determinations proved it to have the double formula C_2H_6. It is also obtained from ethyl iodide, alcohol, and zinc dust, or from zinc ethyl (*Frankland*), hence the name "ethyl hydride". "Ethyl hydride" and "methyl", which were formerly supposed by *Frankland* and *Kolbe* to be different substances, were proved to be identical by *Schorlemmer* in 1863 by their conversion into C_2H_5Cl, which may be prepared from both in exactly the same way.

It is a gas which can be condensed under a pressure of 46 atmospheres at 4°, and is somewhat more soluble than

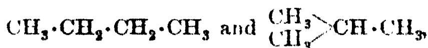
methane in water and alcohol. It burns with a faintly luminous flame.

Propane, C_3H_8, and the two butanes, C_4H_{10}, are also gaseous at the ordinary temperature, and are present to a certain extent in crude petroleum.

Theoretically propane can exist in only one form, represented by the constitutional formula $CH_3 \cdot CH_2 \cdot CH_3$, as this is the only manner in which three carbon and eight hydrogen atoms can be grouped up if we assume that the carbon atoms are tetravalent and the hydrogen atoms monovalent.

ISOMERISM, NOMENCLATURE, CONSTITUTION

To determine whether the next homologue, C_4H_{10}, can theoretically exist in more than one modification, we can start with propane, $\overset{\alpha}{C}H_3 \cdot \overset{\beta}{C}H_2 \cdot \overset{\alpha}{C}H_3$, and replace one of the eight hydrogen atoms by a methyl group. It is obvious that we can obtain two distinct compounds according to whether we replace one of the six terminal hydrogens (α) or one of the central hydrogens (β). The two compounds would have the respective formulæ



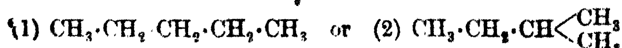
$$CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_3 \text{ and } \begin{matrix} CH_3 \\ CH_3 \end{matrix}\!\!>\!CH \cdot CH_3,$$

and are known as normal butane and iso-butane (or trimethyl methane).

Two compounds having the formula C_4H_{10} are actually known, and their constitutional formulæ derived from their methods of formation agree with the two formulæ $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_3$ and $(CH_3)_2 : CH \cdot CH_3$, as the *n*-compound may be obtained by the action of zinc on ethyl iodide, $CH_3 \cdot CH_2I$, and the *iso*-compound by the reduction of tertiary butyl iodide, $(CH_3)_2 : CI \cdot CH_3$.

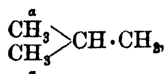
All the succeeding hydrocarbons can, according to theory, exist in various isomeric modifications. The number of modifications possible can be derived in exactly the same manner as already described for the butanes.

As an example, take the hydrocarbons C_5H_{12}, the pentanes. Starting with *n*-butane, $\overset{\alpha}{C}H_3 \cdot \overset{\beta}{C}H_2 \cdot \overset{\beta}{C}H_2 \cdot \overset{\alpha}{C}H_3$, and replacing one H atom by a CH_3 group, we can get either

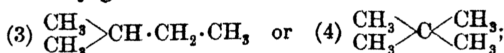


$$(1)\ CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_3 \quad \text{or} \quad (2)\ CH_3 \cdot CH_2 \cdot CH\!<\!\begin{matrix} CH_3 \\ CH_3 \end{matrix}$$

according as we replace an H atom in the α or β position. Starting from iso-butane,



we can similarly get

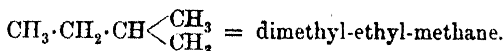


but formulæ (2) and (3) are identical, and the three isomerides possible are therefore $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_3$, $(CH_3)_2 : CH \cdot CH_2 \cdot CH_3$ and $(CH_3)_2 : C : (CH_3)_2$. Of hydrocarbons with six carbon atoms, five isomers are possible, and they are all known. Of the nine possible heptanes, C_7H_{16}, the existence of five has already been proved.

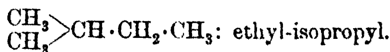
The number of theoretically possible isomers increases very rapidly with the number of carbon atoms, so that, according to *Cayley*, 802 isomeric hydrocarbons of the formula $C_{13}H_{28}$ are possible.

Of these isomers only one can be **normal**, *i.e.* can have a single chain of carbon atoms, in which each of the two terminal carbon atoms is combined with three atoms of hydrogen, and all the middle ones with two, according to the formula, $CH_3 \cdot (CH_2)_n \cdot CH_3$.

A convenient *Nomenclature* for the more complicated paraffins is arrived at by making methane the starting-point for all of them, that carbon atom from which the branching chain emanates being considered as originally belonging to CH_4, in which the hydrogen atoms are supposed to be wholly or partially replaced by hydrocarbon radicals, thus:—



The names of the well-known lower hydrocarbon radicals (alkyls) are also frequently used as a basis; for instance, the group $(CH_3)_2CH$ is termed isopropyl (see Isopropyl Alcohol), hence the compounds:





The boiling-points of the normal hydrocarbons are always

higher than those of the isomers; indeed the boiling-points becomes lowered continuously the more the carbon atom chain is branched, *i.e.* the more methyl groups are gathered together in the molecule.

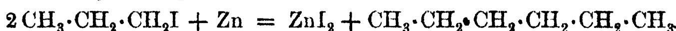
The *Constitution* of the higher paraffins can in most cases only be arrived at with certainty from their synthetical formation (*e.g.* normal butane and hexane), or from their chemical relation to oxygenated derivatives whose constitution is already known, especially to the ketones and acids. (See Ketones.)

If, for instance, by the action of PCl_5 upon acetone, for which the constitution $CH_3 \cdot CO \cdot CH_3$ is proved, the substance $CH_3 \cdot CCl_2 \cdot CH_3$ (acetone chloride) be formed, and this be then treated with zinc methyl, the resulting hydrocarbon, a pentane will have the constitution $(CH_3)_4C$:



$$(CH_3)_2{:}CCl_2 + Zn(CH_3)_2 = ZnCl_2 + (CH_3)_2{:}C{:}(CH_3)_2.$$

As a second example, we have *n*-hexane, which can be obtained by the action of metals upon *n*-propyl iodide, as represented by the equation:



$$2\,CH_3 \cdot CH_2 \cdot CH_2I + Zn = ZnI_2 + CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_3.$$

The system of nomenclature suggested by the International Congress at Geneva is as follows:—The normal paraffins retain their present names. Thus hexane means the compound $CH_3 \cdot (CH_2)_4 \cdot CH_3$. In the case of those with branching chains the longest normal chain gives the name, the branches being regarded as substituents, and the position of substitution being indicated by the successive numbering of the atoms of the carbon chain (the carbon atom which is nearest to the point of ramification is numbered 1; should there be more than one branching—say, a longer and a shorter—then No. 1 begins with the end carbon atom which stands nearest to the shorter branching). Trimethyl-methane is therefore called 2-methyl-propane; dimethyl-ethyl-methane, 2-methyl-butane; and tetramethyl-methane, 2:2-dimethyl-propane.

The following paraffins have been obtained from crude petroleum: *n*- and *iso*-pentane, *n*-hexane and an isomer, and *n*-heptane, all these being present in the so-called "gasoline", which is obtained by the distillation of petroleum, and is used for carburetting coal-gas; further, normal Heptane, *n*-Octane,* *n*-Nonane, and *n*-Decane, besides an isomer of each, and in

* The petroleum ether and ligroïn of commerce consist principally of the hydrocarbons C_6H_{14}, C_7H_{16}, and C_8H_{18}.

addition to these (as also from the distillation of cannel and Boghead coal), a large number of the higher hydrocarbons. In all probability these products are not chemical individuals, but mixtures of homologues and isomers standing very near to each other, as is shown by a comparison with the artificially-prepared normal hydrocarbons.

F. Krafft has prepared those normal hydrocarbons from $C_{11}H_{24}$ to $C_{35}H_{72}$, which are mentioned in the table on p. 30, from the acids C_{12}, C_{14}, C_{16}, and C_{18} of the acetic acid series (see these), for which the normal constitution, *i.e.* non-branching carbon chain, has been demonstrated; and also from the ketones, $C_nH_{2n}O$, which are obtained by subjecting the barium salts of these acids to dry distillation, either alone or together with acetate or heptoate of calcium, and which, as a consequence of their mode of formation, yield normal hydrocarbons. (See Ketones.) *Krafft* has further isolated the normal hydrocarbons $C_{17}H_{36}$ to $C_{23}H_{48}$, also $C_{24}H_{50}$, $C_{26}H_{54}$, and $C_{28}H_{58}$, by subjecting the paraffin obtained from lignite to fractional distillation *in vacuo*.

These are, from about $C_{16}H_{34}$ (m.-pt. 18°) on, solid at the ordinary temperature. When distilled under atmospheric pressure the higher hydrocarbons partially decompose into lower ones of the formulæ C_nH_{2n+2} and C_nH_{2n}; but they may be distilled under reduced pressure. (See Table.)

Mineral Oils.—**Petroleum** and similar products obtained by heating bituminous shale are usually termed mineral oils, in order to differentiate them from vegetable and animal oils, from which they differ in composition.

In many parts of the earth's surface oil rises in the form of springs when bore-holes are made into sand or conglomerate, and the product is the crude petroleum of commerce. Such wells or springs were first discovered in 1859 in Pennsylvania, and since then similar sources have been utilized in the Caspian Sea district (Baku), in Galicia, Roumania, Burma, Assam, Borneo, and South Persia, and in smaller quantities in other parts. In America the oil is accompanied by natural gas consisting largely of the lower paraffin hydrocarbons, and can be used as gaseous fuel. The crude petroleum cannot be used as such, and has to be subjected to a process of fractional distillation and refining by means of sulphuric acid and caustic soda. As a rule, the crude oil is carried long distances to the refining factory, usually in iron pipes 4–8 inches diameter. The pipe line is frequently several hundred miles long, in stages

of 50 miles, with tanks at intervals. The object of the refining is to obtain products of commercial importance and to remove impurities which would affect the values of the fractions, such as tarry or resinous substances and sulphur.

In the American industry a great variety of products is thus obtained, to which different names are given.

	B.P.	Amount.
Cymogene	0°	16·5 per cent.
Rhigoline	18°	
Gasoline	14–90°	
Ligroin	90–120°	
Benzene or Benzoline ...	120–150°	
Kerosene	150–300°	54·0 "
Lubricating oil	...	17·5 "
Vaseline	...	2·0 "
Paraffin wax, m.p.	45–65°	

Liquefied cymogene is used for ice manufacture. Rhigoline is used in medicine as a local anaesthetic. The next three fractions are used for extracting oils and fats and for dry cleaning. **Pentane** b.p. 36° is often isolated and then converted into amyl chloride and finally into amyl alcohol. The *petrol* used in internal-combustion engines usually boils at 70–140°, but at the present time contains less low-boiling constituents than formerly. The kerosene required for illuminating purposes should be water-white, and should not have too low a "flash point". Crude kerosenes and lubricating oils are used for making "oil-gas", small installations of which are used in place of coal-gas. The higher fractions are used as lubricants, and have the advantage over vegetable-oil lubricants; they are chemically inactive, whereas vegetable oils can undergo hydrolysis, and give rise to fatty acids which may have a corroding action on the machinery. These higher oils are also used as fuels; when blown through a nozzle, or "atomizer", in the form of a fine spray they can be burnt under boilers for generating steam, or they may be used in Diesel engines.

The oils are used to such a large extent that the American oil-fields are gradually being worked out in much the same manner as the coal-fields of Britain.

When the oil-wells were first started the chief commercial product was the kerosene, or burning oil, and the lower fractions were largely waste products; the introduction of the internal-combustion engine in automobiles and aeroplanes has created an enormous demand for petrol, and at the present

time the supply can scarcely meet this demand, and other materials have been introduced, one of the most important of which is alcohol. The demand for petrol has also led to the introduction of methods of breaking up the heavier oils by the process of cracking, *i.e.* subjecting the oils to high temperatures, usually under increased pressure, and numerous patents have been taken out. The products vary with the temperature, rate of flow of the oil, construction of the retort, *e.g.* presence of baffle plates and the pressure in the retort. Attempts to crack the higher oil by catalytic agents, such as aluminium chloride, have been tried. The olefines formed during cracking are often absorbed and used for preparing alcohols, *e.g.* ethyl, isopropyl and butyl. In the process of cracking "aromatic hydrocarbons" of the benzene series are often formed. Cf. *Lomas*, *Dunstan* and *Thole*, J. Inst. Petr. Tech., 1914, **1**, 147.

Composition of Natural Petroleum.—The American oil consists mainly of paraffin hydrocarbons, *e.g.* gasolene is largely pentane and hexane, and kerosene contains hydrocarbons from $C_{10}H_{22}$ to $C_{16}H_{34}$. Russian Petroleum, on the other hand, contains appreciable amounts of polymethylene hydrocarbons or naphthenes (Chap. XVI) and of acids derived from them, and gives small yields of low-boiling fractions. Borneo oil contains appreciable amounts of aromatic hydrocarbons, *e.g.* benzene and toluene, &c., and Burma oil is rich in wax.

Origin of Petroleum.—One view is that the oil is formed by the action of steam on carbides of iron and other metals under considerable pressure in the lower portion of the crust of the earth (*Mendelieff*). Another view is that the oil is a product of decomposition of animal or vegetable organisms (*Engler*, C. Z., 1906, II, 1017; compare *Kishner*, J. russ., 1914, **46**, 1428), and this view is supported by the fact that many paraffin oils have a low-optical activity, due probably to the presence of optically active polynaphthenes (C. *Zeit*, 1913, **37**, 550).

The total output of crude petroleum for 1929 was estimated at about 200 million tons, of which 67·6 per cent came from the U.S.A., 9·5 per cent from Venezuela, and 6·8 per cent from Russia.

Shale Oil.—Large quantities of shale oil are distilled in continuous retorts in Scotland, and products analogous to those derived from crude petroleum are obtained, and from low-grade cannel coals or brown coals at suitable temperatures similar products are formed. Such oils differ entirely from the oils obtained from coal in the process of manufacturing coke or coal-gas. (Cf. Chap. XVII, Coal Tar.)

In the manufacture of shale and brown coal oils, appreciable amounts of ammonia are produced. A shale containing 73–80 per cent of mineral matter, yields about 20 gall. of crude oil and 44 lb. of ammonium sulphate per ton of shale.

Paraffin-Wax, obtained by *Reichenbach* in 1830 from wood-tar, is got by the distillation of lignite or peat. It also is a mixture of many hydrocarbons, about 40 per cent of it consisting of the compounds $C_{22}H_{46}$, $C_{24}H_{50}$, $C_{26}H_{54}$, and $C_{28}H_{58}$.

Liquid Paraffin (*Reichenbach's* "Eupion") and the butter-like **Vaseline** are high-boiling distillation products of lignite or petroleum, and the same applies to many lubricating oils. Vaseline is also obtained by decolorizing the residues obtained in distilling crude petroleum.

Ozokerite, green, brown, and red, and of the consistency of wax, melting-point 60–80°, is a natural paraffin found at Boryslaw in Galicia, at Tscheleken near Baku, on the Caspian Sea, and forms the ceresine of commerce when bleached.

Asphalt, or **Earth Pitch**, found in India, Trinidad, Java, and Cuba, is a transformation product of the higher-boiling mineral-oils, produced by the action of the oxygen of the air just as paraffin absorbs oxygen and becomes brown upon prolonged heating in the air. It is used for cements and salves, and in asphalting, photo-lithography, &c.

B. Olefines or Hydrocarbons of the Ethylene Series (Alkylenes): C_nH_{2n}

There are two series of hydrocarbons of the general formula C_nH_{2n}, the members of which differ from the corresponding paraffins by containing two atoms of hydrogen less in the molecule. The one series is that of the **Olefines**, of which ethylene, C_2H_4, is the first member; the other is that which contains **Trimethylene, Tetramethylene, Hexamethylene**, &c. (Cf. Chap. XVI, Polymethylenes.)

The properties exhibited by these two series are so different that different constitutions must be accorded to them. The olefines form additive compounds with exceptional facility, being thus converted into the paraffins or their derivatives; from this the conclusion is drawn that, like the latter, they contain an open carbon chain.

The names given to the hydrocarbons are similar to those for the paraffins, except that the termination *ane* is replaced by *ene*, or often by *ylene*.

SUMMARY

		Melting-point.	Boiling-point.
Ethylene	C_2H_4	−169°	−103°
Propylene	C_3H_6		−48°
Butylene (3)	C_4H_8 α		−5°
	C_4H_8 β		+1°
	C_4H_8 γ		−6°
Amylene (5)	C_5H_{10}*		+39°
Hexylene	C_6H_{12}		68°
Heptylene	C_7H_{14}		95°
Octylene	C_8H_{16}		124°
Nonylene	C_9H_{18}		153°
Decylene	$C_{10}H_{20}$		172°
Undecylene	$C_{11}H_{22}$		195°
Dodecylene	$C_{12}H_{24}$	−31°	{96°†
Tridecylene	$C_{13}H_{26}$		233°
Tetradecylene	$C_{14}H_{28}$	−12°	{127°
Pentadecylene	$C_{15}H_{30}$		247°
Hexadecylene (Cetene)	$C_{16}H_{32}$	+4°	274° / {155°
Octadecylene	$C_{18}H_{36}$	18°	{179°
Eicosylene	$C_{20}H_{40}$		
Cerotene	$C_{27}H_{54}$	58°	
Melene	$C_{30}H_{60}$	62°	

The general formula C_nH_{2n} for this series indicates that each member differs from the corresponding member of the paraffins by two hydrogen atoms.

In their physical properties they resemble the methane homologues very closely. C_2H_4, C_3H_6, and C_4H_8 are gases, C_5H_{10} a volatile liquid, the higher members liquids with rising boiling-point and diminishing mobility, while the highest are solid and similar to paraffins. The boiling-points of members of both series containing the same number of carbon atoms, and whose constitutions are comparable, lie very close together, but the melting-points of the olefines are somewhat the lower of the two; *e.g.* $C_{16}H_{34}$, m.-pt. 21°, b.-pt. {157°, and $C_{16}H_{32}$, m.-pt. 4°, b.-pt. {155°.

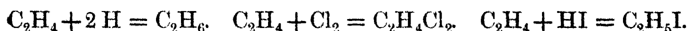
* The melting- and boiling-points given from C_5H_{10} on, are those of the normal hydrocarbons.

† { signifies boiling-point under 15 mm. pressure.

Most of the olefines are readily soluble in alcohol and ether, but insoluble in water, only the lower members dissolving slightly in the latter. The specific gravities of the normal olefines, determined at the melting-points, rise from about 0·63 upwards, and approach with increasing carbon to a definite limit, viz. about 0·79.

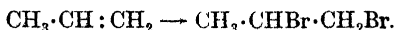
The chemical properties of the olefines are quite different from those of the paraffins. The latter are comparatively inert; they are not readily oxidized, and do not form additive compounds, but can yield substitution products with halogens. The olefines, on the other hand, are chemically reactive. They are *unsaturated*, *i.e.* they can form additive compounds with elements or compounds without a fission of their molecules (cf. Chap. L, A., Unsaturation), and are readily oxidized. These characteristic chemical properties are usually attributed to the presence of a double bond or linking between two carbon atoms, and this is usually termed an olefine linking, *e.g.* $CH_2:CH_2$.

(*a*) *Additive reactions.*—They all combine with H_2, Cl_2, Br_2, HI, HClO, HBrO, N_2O_4, H_2SO_4 (fuming), yielding paraffin hydrocarbons or their derivatives:



$$C_2H_4+2\,H = C_2H_6. \quad C_2H_4+Cl_2 = C_2H_4Cl_2. \quad C_2H_4+HI = C_2H_5I.$$

In all these reactions the double-linking characteristic of the olefines becomes replaced by a single bond, and two monovalent groups or atoms become attached to the carbon atoms which were previously united by the double bond. It follows that a dibromide formed from an olefine and bromine will always have the two bromine atoms attached to adjacent carbon atoms. (Cf. Chap. XVI, Polymethylene Derivatives.)

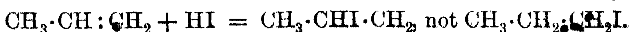


$$CH_3{\cdot}CH:CH_2 \longrightarrow CH_3{\cdot}CHBr{\cdot}CH_2Br.$$

Addition of hydrogen can be effected in a variety of different ways, *e.g.* (*a*) by the use of reducing agents, *i.e.* the addition of nascent hydrogen; sodium amalgam and water are sometimes used for this purpose; (*b*) by passing hydrogen gas into the hydrocarbon in the presence of platinum black or colloidal paladium, which act as catalysts; (*c*) by passing a mixture of the vapour of the hydrocarbon and of hydrogen over finely-divided nickel; (*d*) heating with hydriodic acid (conc.) and phosphorus.

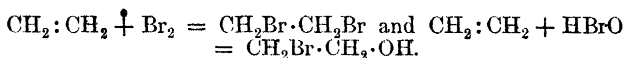
Chlorine combines most readily of the halogens and iodine

least readily; on the other hand, HI adds on more easily than HBr, and this more readily than HCl. It is obvious that when the two addenda are different, *e.g.* HCl, *i.e.* H and Cl or HClO, *i.e.* HO and Cl, and the hydrocarbon is not symmetrical in structure that, theoretically, the addition can take place in two different ways. In reality, it is found that in the majority of cases the addition of halogen hydride is such that the halogen attaches itself to the carbon atom which is united to the smaller number of hydrogen atoms*:



$$CH_3 \cdot CH : CH_2 + HI = CH_3 \cdot CHI \cdot CH_3, \text{ not } CH_3 \cdot CH_2 \cdot CH_2I.$$

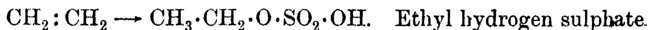
When aqueous solutions of bromine are used the reaction is not simply the addition of bromine and the formation of a dibromide. Part of the bromine reacts with water, forming hypobromous acid, which adds on to the olefine, yielding a bromo-derivative of an alcohol (cf. Chap. L, A.):



$$CH_2 : CH_2 + Br_2 = CH_2Br \cdot CH_2Br \text{ and } CH_2 : CH_2 + HBrO = CH_2Br \cdot CH_2 \cdot OH.$$

(Cf. *Reid* and *Williams*, J. C. S., 1917, **111**, 240; *Bülman*, Rec. Trav., 1917, **36**, 313.) The addition of sodium bromide alters the equilibrium $Br_2 + H_2O = HBr + HBrO$ by favouring the reverse reaction, and hence increases the amount of dibromide formed.

The reaction with sulphuric acid (concentrated or fuming) is complex. (Cf. *Brooks* and *Humphreys*, J. Am. C. S., 1918, **40**, 822.) The products are polymerized olefines, alkyl hydrogen sulphates formed by the addition of H and $O \cdot SO_2 \cdot OH$ to the hydrocarbon, and alcohols:



$$CH_2 : CH_2 \longrightarrow CH_3 \cdot CH_2 \cdot O \cdot SO_2 \cdot OH. \quad \text{Ethyl hydrogen sulphate.}$$

The tendency to form sulphates increases from ethylene to amylene, and then diminishes.

(*b*) They readily polymerize, especially in presence of sulphuric acid or zinc chloride. Thus amylene, C_5H_{10}, in presence of sulphuric acid yields the polymers $C_{10}H_{20}$, $C_{15}H_{30}$, and $C_{20}H_{40}$.

(*c*) Unlike the paraffins, they are readily oxidized by $KMnO_4$ or CrO_3, but not by cold HNO_3.

In this reaction, two hydroxyl groups are added to the

* Cf. *Michael*, J. pr. 1888, [ii] 37, 524; 1903, 68, 487; B. 1906, 39, 2138.

molecule of the olefine if a dilute (1 per cent) solution of permanganate is used, and a dihydric alcohol (a glycol) is formed.



$$CH_2 : CH_2 \longrightarrow OH \cdot CH_2 \cdot CH_2 \cdot OH.$$

But if stronger solutions are used, or if chromic anhydride is employed, the molecule of the olefine is ruptured at the point where the double bond exists and a mixture of simpler acids or ketones is obtained. The readiness with which olefine compounds discharge the colour of acidified permanganate is frequently made use of as a qualitative test for such compounds, but is given by numerous other compounds, in fact by any organic compound which is readily oxidized, *e.g.* an aldehyde, an amine or a phenol.

Nomenclature.—Ethylene was first prepared by four Dutch chemists, who observed that it formed an oil with chlorine, hence they termed ethylene **olefiant gas**, and the name olefine has been given to the whole series of hydrocarbons.

The official names for the various olefines, as suggested by the Geneva Congress, are formed by replacing the last syllable "ane" of the paraffins by "ene". The position of the double bond is denoted by the number of the carbon atom from which it proceeds. In a branching chain the numbering is the same as in the case of the corresponding saturated hydrocarbons; in a normal chain it begins at the end carbon atom which is nearest to the double bond.

The following examples illustrate this system:

$\overset{1}{C}H_3 \cdot \overset{2}{C}H : \overset{3}{C}H \cdot \overset{4}{C}H_2 \cdot \overset{5}{C}H_3$ is 2-pentene or Δ^2-pentene, where Δ denotes the double bond.

$\overset{1}{C}H_3 \cdot \overset{2}{C}H : \overset{3}{C}(CH_3) \cdot \overset{4}{C}H_2 \cdot \overset{5}{C}H_2 \cdot \overset{6}{C}H_3$ is 3-methyl-2-hexene.

$\overset{1}{C}H_3 \cdot \overset{2}{C}H : \overset{3}{C}\!<\!\begin{matrix} \overset{4}{C}H_2 \cdot \overset{5}{C}H_3 \\ \underset{3^1}{C}H_2 \cdot \underset{3^2}{C}H_3 \end{matrix}$ is 3-ethyl-2-pentene.

$\begin{matrix} \overset{1}{C}H_3 \cdot \overset{2}{C}H \\ CH_3 \cdot CH_2 \end{matrix}\!>\!\overset{3}{C} \cdot \overset{4}{C}H(CH_3) \cdot \overset{5}{C}H\!<\!\begin{matrix} \overset{6}{C}H_3 \\ CH_3 \end{matrix}$ is 4:5-dimethyl-3-ethyl-2-hexene.

$\overset{1}{C}H_2 : \overset{2}{C}H \cdot \overset{3}{C}H_2 \cdot \overset{4}{C}\!\begin{matrix} \diagup \overset{5}{C}H_2 \cdot \overset{6}{C}H_2 \cdot \overset{7}{C}H_3 \\ - CH_2 \cdot CH_2 \cdot CH_3 \\ \diagdown CH_2 \cdot CH_3 \end{matrix}$ is 4-ethyl-4-propyl-1-heptene.

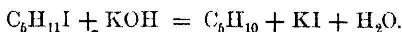
Modes of formation.—(*a*) Together with paraffins by the destructive distillation of many substances, such as wood,

lignite, and coal, and also by the distillation of the higher paraffins (process of "cracking", p. 43); illuminating gas consequently contains the olefines C_2H_4, C_3H_6, C_4H_8, &c.

(*b*) By abstraction of water from the alcohols, $C_nH_{2n+1}OH$, by heating them with sulphuric acid, phosphorus pentoxide, zinc chloride, anhydrous formic acid, syrupy phosphoric acid, *p*-toluenesulphonic acid, &c. With sulphuric acid, an alkyl-sulphuric acid, *e.g.* ethyl hydrogen sulphate, $C_2H_5O \cdot SO_2 \cdot OH$, is first formed, and decomposes into alkylene and sulphuric acid. This method is especially applicable in the case of the lower homologues. Many alcohols yield olefines when heated alone, or with finely divided solids (Chap. XLIX).

The palmitic esters of the higher alcohols, when distilled under somewhat diminished pressure, yield palmitic acid and an olefine.

(*c*) By heating the halogen compounds $C_nH_{2n+1}X$ with alcoholic potash, or by passing their vapour over red-hot lime or hot oxide of lead, &c.; sometimes by simple distillation:



$$C_5H_{11}I + KOH = C_5H_{10} + KI + H_2O.$$

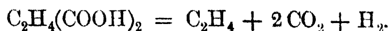
The iodine and bromine compounds are particularly suited for this. The reaction may be regarded as the elimination of a molecule of halogen hydracid from the molecule of the compound, the halogen coming from the one carbon atom and the hydrogen from an adjacent. (Cf. also *Nef*, A. 1901, 318, 3.)

(*d*) Sometimes from the haloid compounds $C_nH_{2n}X_2$ by abstraction of the halogen,* *e.g.* ethylene from ethylene bromide by treatment with zinc, magnesium, or zinc dust and alcohol:



$$C_2H_4Br_2 + Zn = C_2H_4 + ZnBr_2.$$

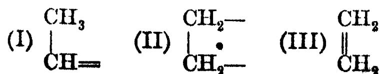
(*e*) By the electrolysis of potassium salts of dibasic acids of the succinic acid series; thus succinic acid itself yields ethylene:



$$C_2H_4(COOH)_2 = C_2H_4 + 2CO_2 + H_2.$$

The complex anion $O \cdot CO \cdot \overline{CH_2} \cdot \overline{CH_2} \cdot CO \cdot O$, when discharged decomposes into ethylene and carbon dioxide.

Constitution of the Olefines.—For ethylene the following formulæ may be given:—



(I) CH_3—$CH=$ (II) CH_2—, CH_2— (III) $CH_2 = CH_2$

* Only when the halogen atoms are attached to adjacent carbon atoms.

In the formulæ I and II, two free carbon bonds or valencies are assumed in the ethylene molecule. Formula III follows from the assumption that the bonds which are not used up in attaching the hydrogen atoms to carbon are used in uniting the carbon atoms themselves.

Now the ethylene bromide which is formed by the addition of bromine to ethylene has, for reasons which will be given under that compound, the constitution $CH_2Br \cdot CH_2Br$, and likewise the compound obtained by the addition of ClOH (*i.e.* Cl and OH), viz. glycol chlorhydrin, the constitution $CH_2Cl \cdot CH_2OH$: consequently formula I, according to which these substances would have the constitutions $CH_3 : CHBr_2$ and $CH_3 \cdot CHCl(OH)$, is excluded.

Formula III is more probable than formula II:—

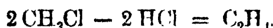
(*a*) Since methylene, CH_2:, appears to be incapable of existence; all attempts to isolate it have yielded ethylene, C_2H_4 (see below), so that free valencies attached to the carbon atom probably cannot exist. Cf., however, Chap. L, D.

(*b*) Because the free affinities to be assumed according to II are never found singly (which should in that case be possible), but invariably in pairs only, and indeed only on neighbouring carbon atoms. This is proved from the constitution of the compounds obtained by the addition, for instance, of Br_2. Unsaturated compounds containing only one carbon atom, and unsaturated hydrocarbons containing an *odd* number of hydrogen atoms, are unknown.

It is therefore to be concluded that in ethylene and its homologues a double carbon bond, corresponding with formula III, exists.

By this term "double bond" is not, however, to be understood a closer or more intimate combination. The olefines, on the contrary, are more readily oxidized than the paraffins, being thereby attacked at the point of the double bond. Other properties, especially physical ones, also give indications that a double bond between two carbon atoms is looser, and therefore more easily broken, than a single one. (Cf. *Brühl*, A. **211**, 162.)

1. **Methylene** (*Methene*), CH_2, does not exist. Numerous attempts to prepare it, *e.g.* by the withdrawal of hydrogen and chlorine from methyl chloride, or of iodine from methylene iodide, have invariably yielded ethylene, thus:—



$$2\,CH_3Cl - 2\,HCl = C_2H_4.$$

Here the two resulting CH_2-residues have united together, in the same way as the two methyl-groups coalesced to ethane (p. 34).

2. **Ethylene** (*Ethene*), olefiant gas, $CH_2:CH_2$.

This compound was discovered in 1795 by four Dutch chemists. Its formula was established by *Dalton*.

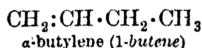
Illuminating gas generally contains 4 to 5 per cent of ethylene. For formation from elements see *Pring* and *Fairlie*, J. C. S. 1911, 99, 1806. It is usually prepared by heating alcohol with excess of concentrated sulphuric acid, with addition of sand or anhydrous aluminium sulphate, a mixture of equal portions of the two liquids being subsequently dropped into the evolution flask; sulphur dioxide, &c., are produced at the same time by secondary reactions. A better method is to heat alcohol with syrupy phosphoric acid at 200° (*Newth*), or to pass alcohol over an hydrous alum. It is further formed by heating ethylidene chloride, $CH_3 \cdot CHCl_2$, with sodium, or ethylene bromide with zinc.

It may be liquefied at 0° under a pressure of 44 atmos., is very slightly soluble in water and alcohol; burns with a luminous flame, and forms an explosive mixture with oxygen. When rapidly mixed with two volumes of chlorine and set fire to, it burns with a dark-red flame, with formation of hydrochloric acid and deposition of much soot. It is converted at a red heat into methane, CH_4, ethane, C_2H_6, acetylene, C_2H_2, &c., with separation of carbon. (See p. 36.) It combines with hydrogen in presence of spongy platinum to ethane, C_2H_6.

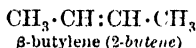
3. **Propylene** (*Propene*), C_3H_6, $CH_2:CH \cdot CH_3$. Only one olefine, C_3H_6, is theoretically possible and only one is known, viz. methylethylene. It can be prepared from isopropyl iodide and caustic potash, or by heating glycerol with zinc dust. It is isomeric with trimethylene (see Polymethylenes).

4. **Butylene**, C_4H_8. Three butylenes are possible according to theory, and three are known. All of them are gaseous, their boiling-points lying between −6° and +3°. Butylene and pseudo-butylene are derived from normal butane, and isobutylene from isobutane, since they severally combine with H_2 to form these hydrocarbons. The first, α-butylene, is prepared from normal; the second, β-butylene, from secondary; and the third, γ-butylene, from tertiary butyl iodide, by the action of caustic potash upon these; the last can also be obtained from isobutyl alcohol and sulphuric acid. The isomerism of the two

butylenes derived from normal butane is explained by the assumption of a double bond at different points, thus:—



$CH_2{:}CH{\cdot}CH_2{\cdot}CH_3$
α-butylene (1-*butene*)



$CH_3{\cdot}CH{:}CH{\cdot}CH_3$
β-butylene (2-*butene*)

Isobutylene has the formula $(CH_3)_2C{:}CH_2$ (*methylpropene*). The behaviour of these isomers upon oxidation is in accordance with the above formulæ, the oxidation always taking place at the point of the double bond.

The butylenes are isomeric with tetra-methylene (*cyclo-butane*; see Polymethylenes).

5. **Amylene**, C_5H_{10}. A large number of isomeric amylenes are known, among them being **Amylene** (b.-pt. 35°), which is obtained, together with an isomer, Iso-amylene, by heating ordinary amyl alcohol with chloride of zinc. For it the constitutional formula $(CH_3)_2C{:}CH{\cdot}CH_3$ (=trimethylethylene) is assumed. This is known in the pure form under the name of "pental".

The higher Olefines of normal constitution, with 12, 14, 16, and 18 atoms of carbon, have been prepared by *Krafft* according to method *b*.

Cerotene and **Melene** (m.-pt. 62°) are obtained by the distillation of Chinese wax and bees'-wax respectively. They are like paraffin in appearance, and are only sparingly soluble in alcohol.

C. Hydrocarbons, C_nH_{2n-2}: Acetylene Series

The hydrocarbons of this series again differ from those of the preceding by containing two atoms of hydrogen less. In physical properties they closely resemble both the latter and those of the methane series; thus the lowest members up to C_4H_6 are gaseous, the middle ones liquid, and the highest solid, and in their melting- and boiling-points they do not differ to any extent from those of the other series with an equal number of carbon atoms. The specific gravities of the normal hydrocarbons C_{12}, C_{14}, C_{16}, and C_{18}, at the melting-point, gradually approach with increasing carbon to a definite limit (0·80), and are somewhat higher than those of the corresponding members of the ethylene series throughout.

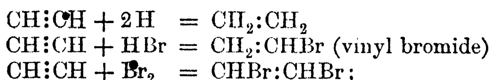
Constitution.—Upon grounds similar to those which have already been explained under ethylene, the constitutional formula for acetylene, C_2H_2, is assumed to be $CH{\vdots}CH$, according to which the carbon atoms are joined together by a triple bond.

For a compound C_3H_4, two constitutional formulæ are possible: $CH\vdots C\cdot CH_3$ (allylene) and $CH_2:C:CH_2$ (allene).

As a matter of fact, two hydrocarbons C_3H_4 do exist, only one of which, allylene, yields metallic compounds. It is therefore to be considered the true homologue of acetylene, containing a triple bond, according to the first of the two above formulæ, while to allene the second formula, with the two double bonds, is to be ascribed. The constitution of the tetrabromopropanes, which are formed from these by the addition of bromine, agrees with this conception.

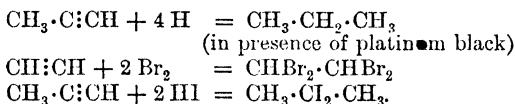
In their chemical relations the acetylenes stand nearer to the olefines than to the paraffins, in so far that they are unsaturated and therefore capable of forming additive products.

1. A molecule of an acetylene can combine either (*a*) with two atoms of hydrogen or halogen, or with one molecule of halogen hydride, to olefines or their substitution products, thus:—



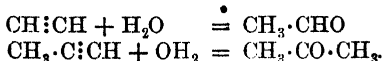
$$CH\vdots CH + 2H = CH_2:CH_2$$
$$CH\vdots CH + HBr = CH_2:CHBr \text{ (vinyl bromide)}$$
$$CH\vdots CH + Br_2 = CHBr:CHBr;$$

or (*b*) with four atoms of hydrogen or halogen, or two molecules of halogen hydride, to paraffins or paraffin substitution products, thus:—



$$CH_3\cdot C\vdots CH + 4H = CH_3\cdot CH_2\cdot CH_3$$
(in presence of platinum black)
$$CH\vdots CH + 2Br_2 = CHBr_2\cdot CHBr_2$$
$$CH_3\cdot C\vdots CH + 2HI = CH_3\cdot CI_2\cdot CH_3.$$

Like many of the olefines, various members of this series combine with water under the influence of dilute acids, thus allylene, C_3H_4, gives acetone, C_3H_6O; and acetylene, C_2H_2, gives crotonic aldehyde, with intermediate formation of acetic aldehyde. The combination with water may be accomplished (*a*) by the action of sulphuric acid when, as in the case of the olefines, alkyl hydrogen sulphates are formed as intermediate products, at 0° under pressure ethylene gives a nearly theoretical yield of ethyl hydrogen sulphate; (*b*) by means of mercuric chloride solution or of mercury and acids; or (*c*) by directly heating the hydrocarbon with water at 300° in sealed tubes.



$$CH\vdots CH + H_2O = CH_3\cdot CHO$$
$$CH_3\cdot C\vdots CH + OH_2 = CH_3\cdot CO\cdot CH_3.$$

2. Many of the acetylene hydrocarbons are readily polymerized; thus, acetylene is transformed into benzene when led through a red-hot glass tube. This is an important synthesis of benzene: $3C_2H_2 = C_6H_6$. At the same time the compounds C_8H_8, $C_{10}H_8$, &c., are formed. Similarly allylene, C_3H_4, gives mesitylene, C_9H_{12}, in contact with sulphuric acid and a little water. (See Benzene Derivatives.)

3. Acetylene and some of its homologues react in a characteristic manner with an ammoniacal solution of cuprous or argentic oxide, to form reddish-brown or yellow-white precipitates; *e.g.* CCu⋮CCu; CAg⋮CAg; CH_3·C⋮CAg, &c., which are explosive, and which are decomposed by acids, such as HCl, with regeneration of the hydrocarbon. The first products formed appear to be additive compounds, *e.g.* C_2H_2, CuCl, and these then yield the substituted derivatives.

The hydrogen of acetylene can be replaced by potassium or sodium, thus, when the hydrocarbon is heated with sodium, the compounds C_2HNa and C_2Na_2 are obtained. These are decomposed by water or acids with evolution of acetylene.

(For syntheses with the aid of acetylene, see Chap. XLIX, H.)

All the hydrocarbons C_nH_{2n-2} do not, however, give such metallic compounds, but only the true homologues of acetylene containing the grouping ·C⋮CH.

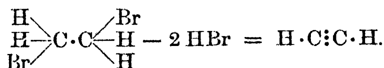
Hydrocarbons such as allene, CH_2:C:CH_2, which do not contain a triple bond, and even acetylene compounds such as CH_3·C⋮C·CH_3, where no hydrogen atoms are attached to the C atoms between which the triple bond is supposed to exist, do not yield these metallic derivatives.

In the case of higher homologues, isomerism may be due either to the difference in position of the triple carbon bond in the molecule, or to the presence and different positions of two double bonds. The constitution of a compound is fixed by the formation or otherwise of metallic derivatives, and by its behaviour upon oxidation. (See Oxidation of the Butylenes, p. 52.)

The official name of the acetylene homologues proper, with a triple carbon-linking, ends in "ine"; that of the isomeric hydrocarbons, with two double bonds, in "diene".

Formation.—1. They are obtained, together with the hydrocarbons already described, by the distillation of wood, lignite, coal, &c.; thus illuminating gas contains acetylene, allylene, and crotonylene.

2. By treating the haloid, preferably the bromine, compounds $C_nH_{2n}X_2$ and $C_nH_{2n-1}X$ with alcoholic potash or sodium ethoxide (C_2H_5ONa):



$$\begin{matrix} H \\ H \\ Br \end{matrix} > C \cdot C < \begin{matrix} Br \\ H \\ H \end{matrix} - 2\,HBr = H \cdot C \vdots C \cdot H.$$

With alcoholic potash, even when excess is used, the reaction tends to stop at the first stage, and a brominated olefine is formed, *e.g.* vinyl bromide (p. 68) from ethylene dibromide; with sodium ethoxide, and elimination of hydrogen bromide proceeds more readily.

Further, from the unsaturated alcohols, $C_nH_{2n-1} \cdot OH$, by the separation of the elements of water from them.

3. By the electrolysis of potassium salts of the acids of the fumaric acid series (*Kekulé*).

4. Certain acetylene hydrocarbons, $R \cdot C \vdots C \cdot CH_3$, when heated with sodium, pass into the sodium compounds of their isomers, $R \cdot CH_2 \cdot C \vdots CH$; on the other hand, when the latter are warmed with alcoholic potash, the opposite reaction takes place (*Fawarsky*, B. **20**, Ref. 781; **25**, Ref. 81; **25**, 2244).

Acetylene (*Ethine*), C_2H_2, was first obtained impure by *E. Davy* from calcium carbide in 1839, and pure by *Berthelot* in 1849. Illuminating gas contains 0·06 per cent. It is synthesised from its elements, when an electric arc is caused to pass between two carbon poles in an atmosphere of hydrogen (*Berthelot*), but other hydrocarbons are formed at the same time (*Bone* and *Jerdan*, J. C. S. 1901, 1042; cf. also *Hutton* and *Pring*, 1906, 1591). It may be obtained from ethylene bromide and sodium ethoxide solution; also by the incomplete combustion of many carbon compounds, for instance, when the gas in a *Bunsen* lamp burns at the base; and from ethane, ethylene, and methane at a red heat, or by the action of the induction spark. (See pp. 36 and 51.) The simplest method of preparation is by the action of water on calcium carbide, the water being allowed to drop gradually on to the carbide:



$$CaC_2 + H_2O = CaO + C_2H_2.$$

It becomes liquid at 1° under a pressure of 48 atmospheres, burns with a luminous and very sooty flame, and has a peculiar disagreeable smell. Its flame has a high illuminating power when burnt in specially-constructed burners, and is now largely made use of as an illuminating agent. It dissolves in its own

volume of water, and in six times its volume of alcohol; is poisonous, combining with the hæmoglobin of the blood. It is decomposed into its elements with detonation by explosive fulminate of silver, and also by the electric spark. It combines with hydrogen to ethane, when heated with the latter in presence of platinum black, or to ethylene, upon treating its copper compound with zinc and ammonia. A mixture of acetylene and oxygen explodes violently when a light is applied to it. Chromic acid oxidizes acetylene to acetic acid; and permanganate of potash to oxalic acid. It combines with nitrogen under the influence of the induction spark to hydrocyanic acid (see this), and detonates upon being mixed with chlorine, but additive products, *e.g.* $C_2H_2Cl_2$, can, however, be prepared. As little as ·005 milligramme of it can be detected by the formation of the dark-red copper compound C_2Cu_2. This latter explodes when struck, or when heated to a little over 100°.

Allylene (*Propine*), $CH_3 \cdot C:CH$, can be prepared from propylene bromide, $CH_3 \cdot CHBr \cdot CH_2Br$. It resembles acetylene.

Allene (*Propadiene*), $CH_2:C:CH_2$, is obtained by the electrolysis of itaconic acid.

Diallyl (*Hexa*-1 : 5-*diene*), $CH_2:CH \cdot CH_2 \cdot CH_2 \cdot CH:CH_2$, is obtained from allyl iodide, $CH_2:CH \cdot CH_2I$, and sodium.

Isomeric with these hydrocarbons are certain hydro-derivatives of aromatic hydrocarbons, *e.g.* tetrahydrobenzene, C_6H_{10}; decahydronaphthalene, $C_{10}H_{18}$. (See Aromatic Compounds.)

Certain diolefines are of importance from their relationship to rubber (cf. open chain terpenes, Chap. XLI, A., and Rubber, Chap. LVI).

D. Hydrocarbons C_nH_{2n-6}

Di-acetylene (*Butadiine*), C_4H_2, or $CH:C \cdot C:CH$. This is prepared by heating the ammonium salt of diacetylene-dicarboxylic acid (see this) with ammoniacal copper solution, whereby it is transformed into the cuprous compound of diacetylene, and then warming this with potassium cyanide. It is a gas of a peculiar odour, which yields a violet-red copper compound and a yellow silver one, the latter exploding upon being rubbed, even when moist. (*Baeyer*, B. **18**, 2269.)

Di-propargyl (1:5-*Hexadiine*), C_6H_6, or $CH:C \cdot CH_2 \cdot CH_2 \cdot C:CH$, is obtained by the conversion of diallyl into its tetrabromide, and the subsequent elimination of four molecules of

hydrogen bromide from each molecule of the tetra-bromide; b. pt. 85°. It gives copper and silver compounds, and takes up eight atoms of bromine, &c. It possesses an especial interest, as it is isomeric with benzene. Another isomeride is 2:4-*Hexadiine*, $CH_3\cdot C\vdots C\cdot C\vdots C\cdot CH_3$. (B. **20**, R. 564.)

An interesting compound is vinylacetylene, $CH\vdots C\cdot CH:CH_2$, containing a double and a triple linking. It is formed from butadiine dibromide by the process of exhaustive methylation. (B. 1913, **46**, 535.)

II. HALIDE SUBSTITUTION PRODUCTS OF THE HYDROCARBONS

A. Halogen Derivatives of the Paraffins

These are to be regarded as paraffin hydrocarbons in which one or more hydrogen atoms have become replaced by one or more halogen atoms.

General Properties.—Only a few of these compounds, *e.g.* CH_3Cl, C_2H_5Cl, and CH_3Br, are gaseous at the ordinary temperature; most of them are liquid, and those with a very large number of carbon atoms in the molecule solid, *e.g.* cetyl iodide, $C_{16}H_{33}I$. The introduction of a halogen atom in any hydrocarbon in place of an atom of hydrogen always tends to raise the boiling-point; the introduction of iodine has the most marked effect, and chlorine the least (cf. Table, p. 59). Those which contain a large number of halogen atoms, *e.g.* CI_4, C_2Cl_6, are solid. Under comparable conditions, the boiling-points of the iodides lie, for each atom of halogen, about 50° (40°–60°), and those of the bromides about 22° (20°–24°), above those of the chlorides.

The lowest members of the series have, in the liquid form, at first a higher specific gravity than water, *e.g.* CH_3I, sp. gr. 2·2, C_2H_5Br, sp. gr. 1·47. With an increasing number of carbon atoms, however, the influence of the halogen diminishes, and they become lighter than water.

The halogen substitution products of the hydrocarbons are very sparingly soluble in water, but readily in, and therefore miscible to any extent with, alcohol or ether; they also dissolve in glacial acetic acid. They often possess a sweet ethereal odour, but this becomes less marked with diminishing volatility. Most of them are combustible; thus methyl and ethyl

chloride burn with a green-bordered flame, while ethyl iodide and chloroform can only be set fire to with difficulty. Many members of the series containing one or two atoms of carbon produce insensibility and unconsciousness when inhaled, *e.g.* $CHCl_3$, $C_2H_3Cl_3$, C_2H_5Br, and C_2HCl_5. The liquid iodine derivatives are readily decomposed, and on exposure to light turn deep-brown in colour, owing to the liberation of free iodine, *e.g.* ethyl iodide liberates iodine and gives C_4H_{10}.

In all these compounds the halogen is more firmly bound than in inorganic salts, so that, for instance, when silver nitrate is added to an aqueous solution of a chlorine compound, *e.g.* chloroform, it causes no precipitation of AgCl. Nevertheless, the halogen is in most cases readily exchangeable for other elements or groups, a circumstance of the utmost importance for many organic reactions. This is especially true for the iodine and bromine compounds, which react more readily than the chlorides, and, on account of their lesser volatility, are easier to work with; thus C_2H_5Br reacts with $AgNO_3$ at the boiling temperature, and C_2H_5I in the cold.

In all these halogen compounds the halogen can be again replaced by hydrogen by inverse substitution, *e.g.* by sodium amalgam, by zinc dust and hydrochloric or acetic acid, or by heating with hydriodic acid. (See p. 33.)

Of fluorine compounds, only a few are known as yet; CH_3F and C_2H_5F are gases.

Nomenclature.—The best system of nomenclature is to regard them as derived from the corresponding hydrocarbons, *e.g.* $CHCl_3$ trichloro-methane, CH_3I mono-iodo-methane, and if necessary to indicate the carbon atoms to which the halogen radicals are attached, *e.g.* $CH_2Cl \cdot CH_2Cl$ 1 : 2-dichloro-ethane,* $CH_3 \cdot CHBr_2$ 1:1-dibromo-ethane, $CH_2Br \cdot CH_2 \cdot CH_2Br$ 1:3-dibromo-propane, $CH_3 \cdot CH(CH_3) \cdot CHBr \cdot CH_2 \cdot CH_2Br$ 2-methyl-3 : 5-dibromo-pentane.

Formation. — 1. By **Substitution.** — *Chlorination and Bromination.* Chlorine and bromine act for the most part as direct substituents (see p. 31). With the gaseous hydrocarbons their action even in the cold is an extremely energetic one (*e.g.* chlorine mixed with methane easily causes an explosion, so that dilution with CO_2 is necessary); the higher members require to be heated.

* This is identical with ethylene dichloride. It should never be termed dichloroethylene, which is CHCl : CHCl, a substitution product of ethylene.

HALOGEN SUBSTITUTION PRODUCTS

Saturated Compounds

(*a*) *Mono-substituted Derivatives.*

	Chloride.		Bromide.		Iodide.	
	B.-p.	Sp. gr.	B.-p.	Sp. gr.	B.-p.	Sp. gr.
Methyl........	−23·7°	0·952	+4·5°	1·732	+45°	2·293
Ethyl..........	+12·2°	0·918	38·4°	1·468	72·3°	1·944
n-Propyl......	46·5°	0·912	71°	1·383	102·5°	1·786
iso-Propyl....	36·5°	0·882	60°	1·340	89°	1·744
Prim. *n*-Butyl	78°	0·907	101°	1·305	130°	1·643

(*b*) *Di-substituted Derivatives.*

	Chloride.		Bromide.		Iodide	
	B.-p.	Sp. gr.	B.-p.	Sp. gr.	B.-p.	Sp. gr.
Methylene ...	42°	1·337	97°	2·498	180°	3·292
Ethylene......	84°	1·260	131°	2·189	solid; m.-p. 81–82	
Ethylidene...	58°	1·189	110°	2·080	178°	2·84

(*c*) *Tri-substituted Derivatives.*

	Chloroform.	Bromoform.	Iodoform.
CHX_3.................	b.-p. 61°	b.-p. 151°	melts at 119° sublimes

(*d*) *Tetra-substituted Derivative.*

	Chloride.	Bromide.
CX_4............... Carbon tetra-	76°	solid; m.-p. 92°; b.-p. 189°

Unsaturated Compounds

	Chloride.	Bromide.	Iodide.
Vinyl, $CH_2{:}CHX$	−18°	+23°	56°
Allyl, $CH_2{:}CH{\cdot}CH_2X$	46°	70°	101°

Trichlorethylene boils at 88°, tetrachlorethylene at 121°. Monochlor- and monobrom-acetylene are gaseous.

Compounds of the type CCl_3Br, CCl_2Br_2, CCl_2I_2, &c., are also known.

The first halogen atom enters most easily into the compound, the substitution becoming more difficult as the number of those atoms present increases. In the case of the higher hydrocarbons, two isomeric mono-substitution products are usually formed. The action of the halogens is further facilitated by sunlight, and by the presence of iodine, this latter acting as a carrier of chlorine by the alternate formation of ICl_3 and ICl, thus: $ICl_3 = ICl + 2\,Cl$. Antimony penta

chloride and ferric chloride act in the same way (and also for brominating and iodating,—B. **18**, 2017; A. **231**, 195); iron wire is especially useful in brominating (B. **24**, 4249). When complete chlorination is required, the substance in question is repeatedly saturated with chlorine in presence of iodine, and heated in a tube to a high temperature.

From methane are formed the whole series of substitution products up to CCl_4.

Ethane first yields ethyl chloride, C_2H_5Cl, then ethylidene chloride, $C_2H_4Cl_2$, and so on up to C_2Cl_6.

From propane is first produced normal propyl chloride, C_3H_7Cl, and finally C_3Cl_8. The latter decomposes, upon vigorous chlorination, first into C_2Cl_6 and CCl_4, and the perchloro-ethane subsequently into two molecules CCl_4. On chlorinating butane and the higher hydrocarbons strongly, an analogous splitting up of the molecule is effected. Strong chlorination or bromination readily gives rise at the same time to hexachloro- or hexabromo-benzene.

Iodine seldom acts as a direct substituent, since by this reaction hydrogen iodide would be formed, which would then reduce the iodine compound back to the hydrocarbon. (See p. 33.) To induce the action, therefore, the HI formed must be removed by HIO_3 or HgO. The iodine substitution products of the hydrocarbons are usually prepared indirectly (according to 2 or 3).

2. From **Unsaturated Hydrocarbons.** These combine readily with halogen or halogen hydride. (See p. 46.)

Ethylene gives with hydrochloric, hydrobromic, and hydriodic acids, ethyl chloride, &c., *i.e.* mono-substitution products of ethane; with chlorine, &c., it gives di-substitution products.

The compound $C_2H_4Cl_2$, obtained by the action of chlorine, is called ethylene chloride, has the constitutional formula $CH_2Cl \cdot CH_2Cl$, and is isomeric with the ethylidene chloride $CH_3 \cdot CHCl_2$, obtained by the chlorination of C_2H_5Cl. (For an explanation of this isomerism, see p. 65.)

Propylene combines with hydriodic acid to isopropyl iodide, C_3H_7I, which is reconverted into propylene by elimination of HI. But the same propylene results from a compound isomeric with isopropyl iodide, viz. normal propyl iodide (and also, of course, from the above-mentioned normal propyl chloride), by the elimination of hydrogen iodide (or chloride), so that by this reaction normal propyl iodide can be transformed into isopropyl iodide. (See p. 63.) From the three butylenes there

are formed two butyl iodides, viz. secondary and tertiary, which, as well as the two other existing butyl iodides, yield these butylenes again with alcoholic potash; in this way the two last-mentioned butyl iodides are convertible into their isomers, the two first (see p. 64).

A study of the constitution of the compounds formed, shows that in these additive reactions the *halogen invariably attaches itself to that carbon atom with which are combined the least number of hydrogen atoms*, e.g.

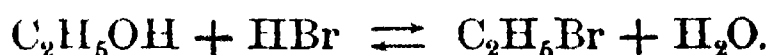


$$CH_3{\cdot}CH{:}CH_2 + HI = CH_3{\cdot}CHI{\cdot}CH_3 \ (\textit{not}\ CH_3{\cdot}CH_2{\cdot}CH_2I);$$

from C_3H_7X onwards, therefore, we obtain only "secondary" and "tertiary" * compounds.

3. From **Compounds containing oxygen.**

(*a*) From the alcohols $C_nH_{2n+1}OH$. In these the OH is readily exchangeable for chlorine, bromine, or iodine by the action of halogen hydride, thus:—



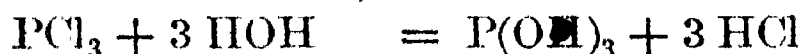
$$C_2H_5OH + HBr \rightleftarrows C_2H_5Br + H_2O.$$

In such exchange the halogen takes the place of the hydroxyl, so that the constitution of the halide product corresponds with that of the alcohol used.

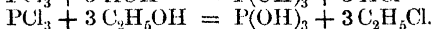
These reactions are reversible or balanced, and a state of equilibrium is reached; according to the law of mass action, it is therefore necessary either to use a large excess of halogen hydride, or to remove the water formed, by sulphuric acid, zinc chloride, &c.

Methyl and ethyl chlorides are easily prepared by distilling the corresponding alcohol with common salt and sulphuric acid, or by leading hydrogen chloride into the warm alcohol containing half its weight of zinc chloride in solution (*Groves*).

The chlorides of phosphorus react in much the same way with alcohols as with water, thus:



$$PCl_3 + 3\,HOH \quad = P(OH)_3 + 3\,HCl$$



$$PCl_3 + 3\,C_2H_5OH = P(OH)_3 + 3\,C_2H_5Cl.$$

The reaction consists in first replacing the chlorine atoms by $O{\cdot}C_2H_5$ groups. The ethyl phosphite, $P(OC_2H_5)_3$, so formed then gives C_2H_5Cl and $P(OH)(OC_2H_5)_2$, and finally $P(OH)_3$ (Abs., 1918, i. 477).

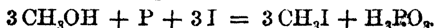
* The names "primary", "secondary", and "tertiary" compounds are founded upon those of the alcohols—primary, secondary, and tertiary in question, from which they can be prepared according to method 3, *a*.

Phosphorus pentachloride is most frequently used for this purpose,



$$PCl_5 + C_2H_5OH = C_2H_5Cl + HCl + POCl_3.$$

Phosphorus oxychloride itself is also sometimes employed. Of especial importance here is the application of the halogen compounds of phosphorus in the production of bromine and iodine compounds. The former need not be prepared beforehand, the end being achieved by gradually bringing phosphorus and iodine or bromine together in presence of the alcohol:



$$3\,CH_3OH + P + 3\,I = 3\,CH_3I + H_3PO_3.$$

This is the method usually employed for the preparation of methyl and ethyl iodides.

(*b*) The halogen derivatives may also be prepared from polyhydric alcohols, *e.g.* trichlorhydrin, $C_3H_5Cl_3$, from glycerol, $C_3H_5(OH)_3$, and PCl_5; isopropyl iodide, C_3H_7I, or allyl iodide, C_3H_5I, from glycerol and PI_3 according to the conditions of the experiment (see p. 63); hexyl iodide, $C_6H_{13}I$, from mannitol, $C_6H_8(OH)_6$ and HI, the latter acting here as a reducing agent also.

(*c*) From aldehydes and ketones (see these), dichloro-substitution products are formed by the action of PCl_5, *e.g.* ethylidene chloride, $CH_3{\cdot}CHCl_2$, from aldehyde, $CH_3{\cdot}CH{:}O$; acetone chloride, $CH_3{\cdot}CCl_2{\cdot}CH_3$, from acetone $CH_3{\cdot}CO{\cdot}CH_3$.

4. Chlorine and bromine compounds are frequently formed from the corresponding iodine or bromine ones by direct exchange, *e.g.* isopropyl bromide from the iodide, or methylene bromide from methylene iodide; (also by treatment with mercuric chloride, stannic chloride, or fuming hydrochloric acid). Conversely the chlorides and bromides may be transformed into the iodides by heating with sodium iodide in alcoholic or acetone solution (B. **18**, 519), dry calcium iodide (B. **16**, 392), or with fuming hydriodic acid.

MONO-SUBSTITUTION PRODUCTS

The **methyl and ethyl** compounds are usually obtained from the corresponding alcohols by one or other of the following methods:—(*a*) Grove's method (p. 61); (*b*) action of concentrated sulphuric acid and sodium halide; (*c*) phosphorus and halogen.

Methyl chloride is often obtained by heating trimethylamine hydrochloride at 360°. (For physical properties, see

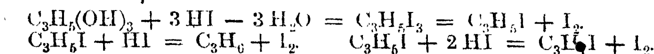
Table.) Methyl chloride is used for the prodnction of artificial cold, for extracting perfumes from flowers, and for methylating dyes in the colour industry. It burns with a green-bordered flame.

Ethyl Fluoride, C_2H_5F. A gas of ethereal odour, which liquefies at $-48°$; it burns with a blue flame, and does not attack glass.

Each **Propyl halide,** C_3H_7X, exists in two isomeric forms, the normal propyl and the isopropyl compounds, the former boiling at a somewhat higher temperature than the latter. To the normal compounds the constitutional formula $CH_3 \cdot CH_2 \cdot CH_2X$ is ascribed, and to the iso-compounds the formula $CH_3 \cdot CHX \cdot CH_3$, since they are derivable respectively from normal propyl alcohol and from isopropyl alcohol or acetone, the constitutions of which can readily be determined.

According to theory only these two cases are possible, since propane, $CH_3 \cdot CH_2 \cdot CH_3$, contains but two types of hydrogen atoms, viz.: (1) six combined with the end carbon atoms, and (2) two combined with the middle ones. For the transformation of the normal into the iso-compounds, see p. 60.

Isopropyl iodide, 2-iodopropane, is prepared from glycerol, phosphorus, iodine, and water (see p. 62); allyl iodide (p. 68) is formed as intermediate product, and at the same time some propylene (p. 51):



$$C_3H_5(OH)_3 + 3\,HI - 3\,H_2O = C_3H_5I_3 = C_3H_5I + I_2.$$
$$C_3H_5I + HI = C_3H_6 + I_2. \qquad C_3H_5I + 2\,HI = C_3H_7I + I_2.$$

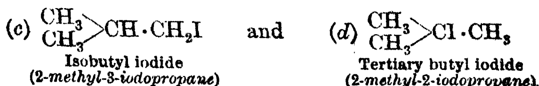
Each **Butyl-halide compound,** C_4H_9X, is known in four isomeric forms, which differ from one another in boiling-point (up to 30°).

Four isomers are theoretically possible; thus from normal butane, $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_3$, are derived:



(*a*) $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2I$ Normal butyl iodide (1-*iodobutane*) and (*b*) $CH_3 \cdot CH_2 \cdot CHI \cdot CH_3$ Secondary butyl iodide (2-*iodobutane*).

according to whether a "terminal" or "central" hydrogen atom is replaced; similarly from trimethylmethane, $CH(CH_3)_3$, are derived:



(*c*) $\frac{CH_3}{CH_3}{>}CH \cdot CH_2I$ Isobutyl iodide (2-*methyl-3-iodopropane*) and (*d*) $\frac{CH_3}{CH_3}{>}CI \cdot CH_3$ Tertiary butyl iodide (2-*methyl-2-iodopropane*).

The constitutions of these four compounds follow from

those of the four corresponding butyl alcohols (p. 70), from which they can be prepared by the action of halogen hydride.

Isobutyl bromide changes into the tertiary compound when heated at 230°–240°, or when kept, probably owing to the intermediate formation of butylene.

The Isobutyl **compounds are the easiest to prepare** (from isobutyl alcohol). **The Tertiary** readily react with H_2O to form the alcohol and halogen hydride, this taking place even in the cold in the case of the iodide.

These mono-halogen derivatives are one of the most important groups of reagents employed by the organic chemist, on account of the readiness with which the halogen atoms may be replaced by other radicals.

Some of the more characteristic reactions are:—

1. Replacement of halogen by hydrogen. Inverse substitution (see p. 33).

2. Replacement of halogen by OH (hydroxyl) (p. 74),



$$C_2H_5I + H_2O = C_2H_5OH + HI,$$

generally by the aid of aqueous alkali, moist silver oxide, or lead oxide and water.

3. Alkalis in alcoholic solution, or alcoholic solutions of sodium methoxide ($CH_3 \cdot ONa$) or sodium ethoxide ($C_2H_5 \cdot ONa$), as a rule, eliminate halogen hydracids, and yield olefines, $CH_2I \cdot CH_3 - HI = CH_2{:}CH_2$. For the reaction it is necessary that the halogen derivative contain at least two carbon atoms, and that a hydrogen atom should be attached to a carbon atom adjacent to the one to which the halogen is united.

4. The halogen may be replaced by the **amino** group $\cdot NH_2$ by the aid of ammonia under pressure, by the **nitro** group $\cdot N{<}^{O}_{O}$ or nitrite radical $\cdot O \cdot N{:}O$ (p. 97), and by the **nitrile** radical $\cdot C{\vdots}N$ (p. 104).

For their use as synthetical reagents, see pp. 125, 236, 245.

DI-SUBSTITUTION PRODUCTS

Methylene chloride, CH_2Cl_2, **Methylene bromide**, CH_2Br_2, and **Methylene iodide**, CH_2I_2, are colourless liquids which are obtained either from the tri-haloid substitution products by inverse substitution, or from the mono-substitution products by the introduction of more halogen. (See table, p. 59.)

The compounds $C_2H_4X_2$ are known in two isomeric forms, to which are assigned the constitutional formulæ:



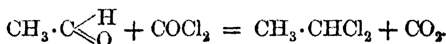
$CH_2X \cdot CH_2X$ (ethylene) and $CH_3 \cdot CHX_2$ (ethylidene).

The former result from the addition of halogen to ethylene, or from the action of halogen hydride or phosphorus haloids upon glycol, $C_2H_4(OH)_2$ (see this), *e.g.* ethylene bromide, by passing ethylene into bromine and water at the ordinary temperature.

The ethylene compounds yield acetylene with alcoholic potash, or better, alcoholic solution of sodium ethoxide, and are transformed into glycol by exchanging their halogen atoms for hydroxyl under the influence of potassium carbonate solution. Glycol, $CH_2(OH) \cdot CH_2 \cdot OH$, with hydrochloric acid yields glycol mono-chlorhydrin, $CH_2Cl \cdot CH_2 \cdot OH$, and this on oxidation yields mono-chloracetic acid, $CH_2Cl \cdot CO \cdot OH$. In this acid it can be shown that the chlorine and hydroxyl radicals are attached to distinct carbon atoms; hence in glycol the two hydroxyl groups, and in ethylene dibromide the two bromine atoms, are almost certainly united to distinct and not to the same carbon atoms.

The **Ethylidene compounds** are obtained from aldehyde (para-aldehyde) by exchange of the oxygen for halogen by means of phosphorus chloride, &c.

Ethylidene chloride, also called ethidene chloride, or 1:1-dichloroethane, is, however, most conveniently prepared with phosgene, $COCl_2$, thus:—



$$CH_3 \cdot C \lessgtr^{H}_{O} + COCl_2 = CH_3 \cdot CHCl_2 + CO_2.$$

It is also formed by the further chlorination of C_2H_5Cl, and is a by-product in the manufacture of chloral. Its boiling-point (57°) is lower than that of ethylene chloride (84°). It is an anæsthetic.

Propylene chlorides, $C_3H_6Cl_2$, bromides and iodides, are likewise known. One group is formed by the addition of halogen to propylene, and thus has an unsymmetrical constitution, *e.g.* propylene chloride, 1 : 2 - dichloropropane, $CH_3 \cdot CHCl \cdot CH_2Cl$. Isomeric with this group are the symmetrically-constituted **Trimethylene derivatives**, of which trimethylene-bromide, 1:3-dibromo-propane, $CH_2Br \cdot CH_2 \cdot CH_2Br$, results from the addition of hydrobromic acid to allyl bromide:



$$CH_2{:}CH \cdot CH_2Br + HBr = CH_2Br \cdot CH_2 \cdot CH_2Br.$$

TRI-SUBSTITUTION PRODUCTS

Chloroform, $CHCl_3$ (*Liebig* and *Soubeiran*, 1831; formula established by *Dumas*, 1835).

Formation.—Of theoretical interest is its formation from methane or methyl chloride. A common method of preparation is by the action of bleaching powder on alcohol or acetones. An improved method is the saturation of alcohol with chlorine and treatment of the product with lime and a little bleaching powder. To obtain pure chloroform on a small scale, chloral or its hydrate is warmed with alkali solution, $CCl_3{\cdot}CHO + NaOH \rightarrow CHCl_3 + H{\cdot}COONa$. It is highly probable that aldehyde and chloral are intermediate products when alcohol is used. It can also be obtained electrolytically from alcohol or acetone and alkali or alkali-earth chloride solutions (Z. Elec., 1919, **25**, 115).

It is a colourless liquid of a peculiar ethereal odour and sweetish taste, is sparingly soluble in water, and solidifies below −70°. B.-pt. 61·2°. Sp. gr. 1·527. It dissolves fats, resins, caoutchouc, iodine, &c., and is also a most valuable anæsthetic (*Simpson*, Edinburgh, 1848).

The carbylamine reaction (see Iso-nitriles) furnishes a delicate test for the presence of chloroform.

Bromoform, $CHBr_3$, is sometimes present in commercial bromine.

Iodoform, CHI_3 (*Serullas*, 1822; formula established by *Dumas*), is prepared by warming alcohol with iodine and alkali or alkaline carbonate:



$$C_2H_5OH + 4I_2 + 6KOH = CHI_3 + HCO_2K + 5KI + 5H_2O.$$

It can also be prepared in the same way from acetone, aldehyde, lactic acid, and, generally, from compounds which contain the group $CH_3{\cdot}CH(OH){\cdot}C$, or $CH_3{\cdot}CO{\cdot}C$ (*Lieben*).

An electrolytic method consists in passing a current through a solution containing potassium iodide, sodium carbonate, and alcohol, the temperature being kept at 65°. Some 85 per cent of the potassium iodide is thus converted into iodoform.

It crystallizes in yellow hexagonal plates, melts at 119°, has a peculiar odour, is volatile with steam, and is an important antiseptic. It contains only 0·25 per cent H, which at first caused the presence of the latter to be overlooked.

Methyl chloroform, $CH_3{\cdot}CCl_3$. This compound, the trichloride of acetic acid, also acts as an anæsthetic.

Glyceryl chloride, *Trichlorhydrin*, 1:2:3-trichloropropane, $CH_2Cl \cdot CHCl \cdot CH_2Cl$, is obtained from glycerol and PCl_5 (p. 62). B.-pt. 158°. The corresponding bromine compound is also known, but not the iodine one, $C_3H_5I_3$, which decomposes in the nascent state (*i.e.* when glycerine, phosphorus, and iodine react together) into allyl iodide, C_3H_5I, and I_2.

HIGHER SUBSTITUTION PRODUCTS

Carbon tetrachloride, CCl_4. Can be prepared from chloroform or carbon disulphide and chlorine. It is a colourless liquid, boils at 77°, and is used as a solvent for fats, &c.

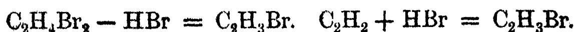
Perchloro-ethane, C_2Cl_6. Rhombic plates of camphor-like odour. Melts and sublimes at 185°.

The chemical properties of these polyhalogen derivatives are somewhat similar to those of the monohalogen derivatives. They may be reduced, transformed into the corresponding alcohols, or the halogen atoms replaced by NH_2 radicals, &c. The action of alkalis on the polyhalogen derivatives, in which the halogen atoms are attached to the same carbon atom, is interesting, *e.g.* CH_2Cl_2 gives not $CH_2{<}^{OH}_{OH}$, but $CH_2{:}O$ formaldehyde and H_2O; $CHCl_3$ gives not $CH(OH)_3$, but this compound $-$water, viz. $O{:}CH \cdot OH$, formic acid. Similarly, CCl_4 gives not $C(OH)_4$, but $CO_2 + 2H_2O$, and $CH_3 \cdot CHBr_2$ gives $CH_3 \cdot CH(OH)_2 - H_2O$, *i.e.* $CH_3 \cdot CHO$.

Many of these reactions require high temperatures; the substances must be heated with the alkali in sealed tubes under pressure. It is characteristic of carbon derivatives that **compounds which contain two or more hydroxyl radicals attached to the same carbon atom are unstable**, and, as a rule, immediately eliminate water yielding an aldehyde, acid, &c. Ammonia and chloroform at a red heat yield HCN and HCl.

B. Halide Derivatives of the Unsaturated Hydrocarbons

These compounds are obtained either by eliminating part of the halogen as halogen hydride from the di-halogen derivatives of the saturated hydrocarbons, or by incompletely saturating the hydrocarbons poorer in hydrogen with halogen or halogen hydride, *e.g.*:



$$C_2H_4Br_2 - HBr = C_2H_3Br. \quad C_2H_2 + HBr = C_2H_3Br.$$

The allyl compounds, C_3H_5X, are obtained from allyl alcohol and halogen hydride or phosphorus halides.

These unsaturated products are very similar to the corresponding saturated ones, but they are, of course, capable of combining further with halogen or halogen hydride, and they exist in stereo-isomeric modifications. (See Fumaric Acid.)

In the unsaturated compounds the halogen atoms are, as a rule, not so readily replaced by other radicals, *e.g.* OH, NH_2, as in the saturated halogen derivatives.

Vinyl bromide, *bromo-ethylene*, $CH_2:CHBr$, is usually prepared from ethylene di-bromide and alkali.

Allyl-chloride, -bromide, and **-iodide**, *3-iodo-1-propene*, $CH_2:CH\cdot CH_2X$, are of importance on account of their relation to the allyl compounds found in nature, *e.g.* oil of mustard and oil of garlic. The iodide is prepared from glycerol, phosphorus, and iodine, and from it, by means of $HgCl_2$, the chloride.

Isomeric with these are the **propylene compounds**, *e.g.* **α-chloro-propylene** (*1-chloro-1-propene*), $CHCl:CH\cdot CH_3$.

Trichloroethylene (*Westrosol*), $CCl_2:CHCl$, a heavy liquid boiling at 88°, is an important solvent for fats, and is formed by the action of dilute alkalis on **acetylene tetrachloride,** $CHCl_2\cdot CHCl_2$, a product formed by the union of acetylene and chlorine (Chap. L, H.).

From acetylene are formed the *Grignard* reagents, $CH\vdots CMgBr$ and $BrMg\cdot C\vdots C\cdot MgBr$, which are used for synthesizing unsaturated alcohols and glycols (Abs., 1914, **i**, 393, 401, 405).

III. MONOHYDRIC ALCOHOLS, OR ALKYL HYDROXIDES

Alcohols may be regarded as paraffins in the molecules of which one or more hydrogen atoms have been replaced by one or more monovalent *hydroxyl* groups, $\cdot O\cdot H$. The $\cdot O\cdot H$ group is thus characteristic of alcohols. For the proof of the presence of the OH group, see p. 17. They are usually divided into groups, according to the number of such radicals contained in the molecule: *dihydric, e.g.* $C_2H_4(OH)_2$; *trihydric, e.g.* $C_3H_5(OH)_3$; *hexahydric, e.g.* $C_6H_8(OH)_6$, &c.

The monohydric alcohols are either saturated or unsaturated, according to the hydrocarbons from which they are derived. The unsaturated closely resemble the saturated, except that they are capable of forming additive compounds.

A. Monohydric Saturated Alcohols, $C_nH_{2n+1}OH$

(See Table, p. 70.)

The lowest members of this series are colourless mobile liquids, the middle ones are more oily, and the highest—from dodecyl alcohol, $C_{12}H_{25}OH$, onwards—are solid at the ordinary temperature, and like paraffin in appearance. Gaseous alcohols are unknown; and it is thus obvious that the introduction of OH for H raises the boiling-point of a substance. Compare—

	B.-p.			B.-p.
CH_4	$-164°$	....	CH_3OH	66°
C_2H_6	$-93°$	....	C_2H_5OH	78°
$C_2H_5(OH)$	78°	....	$C_2H_4(OH)_2$	197°

With compounds of analogous constitution the boiling-point rises with tolerable regularity; in the case of the lower members by about 19°, and higher up in the series by a smaller number.

The lowest members are miscible with water, but this solubility rapidly diminishes as the molecular weight increases; thus butyl alcohol requires 12 parts, and amyl alcohol 40 parts of water for solution, while the higher members are no longer soluble in water. The former can be separated or "salted out" from their aqueous solution by the addition of salts, *e.g.* K_2CO_3 and $CaCl_2$.

The specific gravity is always < 1. The highest members (over C_{16}) can be distilled undecomposed only in a vacuum; at the ordinary pressure they break up into olefine and water. The lowest members possess a spirituous odour, those with more than five C atoms an odour of fusel, and both have a burning taste, while the highest members are like paraffin in appearance and without either taste or smell.

CONSTITUTION AND ISOMERS; CLASSIFICATION OF THE ALCOHOLS

Propyl alcohol, $C_3H_7 \cdot OH$, and the higher members exist in different isomeric modifications; thus there are two propyl, four butyl, and eight amyl alcohols, &c.

The number of isomeric forms theoretically possible can be determined by taking the formulæ for the corresponding saturated hydrocarbons, and seeing in how many different positions

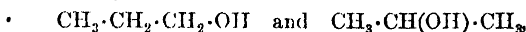
NORMAL MONOHYDRIC SATURATED ALCOHOLS

Name.	Syst. Name.	Const. Formula.	Melting-pt.	Boiling-pt.	Sp. gr. at 0°.
Methyl alcohol	Methan-1-ol	$CH_3 \cdot OH$	...	66°	0·812
Ethyl alcohol	Ethan-1-ol	$CH_3 \cdot CH_2 \cdot OH$	− 130°	78°	0·806
n-Propyl alcohol	Propan-1-ol	$CH_3 \cdot [CH_2]_2OH$	...	97°	0·817
n-Butyl alcohol	Butan-1-ol	$CH_3[CH_2]_3OH$	...	117°	0·823
n-Amyl alcohol	Pentan-1-ol	$CH_3[CH_2]_4OH$	...	138°	0·829
n-Hexyl alcohol	Hexan-1-ol	$CH_3[CH_2]_5OH$	...	157°	0·833
n-Heptyl alcohol	Heptan-1-ol	$CH_3[CH_2]_6OH$	...	176°	0·836
n-Octyl alcohol	Octan-1-ol	$CH_3[CH_2]_7OH$	...	195°	0·839
n-Nonyl alcohol	Nonan-1-ol	$CH_3[CH_2]_8OH$	− 5°	213°	0·842
n-Decyl alcohol	Decan-1-ol	$CH_3[CH_2]_9OH$	+ 7°	231°	0·839
n-Dodecyl alcohol	Dodecan-1-ol	$CH_3[CH_2]_{11}OH$	24°	...	0·831 at 24°

ISOMERIC PROPYL, BUTYL, AND AMYL ALCOHOLS

Name.	Syst. Name.	Const. Formula.	B.-pt.	Sp. gr. at 20°.
Propyl alcohols—$C_3H_7 \cdot OH$.				
Normal	Propan-1-ol	$CH_3 \cdot CH_2 \cdot CH_2 \cdot OH$	97°	0·804
Iso or secondary	Propan-2-ol	$CH_3 \cdot CH(OH) \cdot CH_3$	81°	0·789
Butyl alcohols—$C_4H_9 \cdot OH$.				
Norm. primary	Butan-1-ol	$CH_3 \cdot [CH_2]_3 \cdot OH$	117°	0·810
Norm. secondary	Butan-2-ol	$CH_3 \cdot CH_2 \cdot CH(OH) \cdot CH_3$	110°	...
Prim. isobutyl	2-Methyl-propan-1-ol	$(CH_3)_2 \cdot CH \cdot CH_2 \cdot OH$	107°	0·806
Tertiary	2-Methyl-propan-2-ol	$(CH_3)_3C \cdot OH$	83°	0·786
Amyl alcohols—$C_5H_{11} \cdot OH$.				
Norm. primary	Pentan-1-ol	$CH_3[CH_2]_4 \cdot OH$	138°	...
Isobutyl carbinol	2-Methyl-butan-4-ol	$(CH_3)_2 \cdot CH \cdot CH_2 \cdot CH_2 \cdot OH$	131°	...
Secondary butyl carbinol	2-Methyl-butan-1-ol	$CH_3 \cdot CH_2 \cdot CH(CH_3) \cdot CH_2 \cdot OH$	128°	...
Methyl-propyl carbinol	Pentan-2-ol	$CH_3 \cdot CH_2 \cdot CH_2 \cdot CH(OH) \cdot CH_3$	119°	...
Methyl-isopropyl carbinol	2-Methyl-butan-3-ol	$(CH_3)_2 \cdot CH \cdot CH(OH) \cdot CH_3$	112·5°	...
Diethyl carbinol	Pentan-3-ol	$CH_3 \cdot CH_2 \cdot CH(OH) \cdot CH_2 \cdot CH_3$	117°	...
Dimethyl-ethyl carbinol	2-Methyl-butan-2-ol	$(CH_3)_2 \cdot C(OH) \cdot CH_2 \cdot CH_3$	102°	...

the OH group can be introduced, *e.g.* $CH_3\cdot CH_2\cdot CH_3$, propane, can obviously give—



$$CH_3\cdot CH_2\cdot CH_2\cdot OH \quad \text{and} \quad CH_3\cdot CH(OH)\cdot CH_3,$$

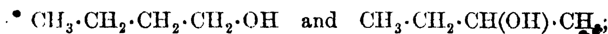
two distinct propyl alcohols.

Butane exists in two forms:



$$CH_3\cdot CH_2\cdot CH_2\cdot CH_3 \text{ or } \textit{normal} \quad \text{and} \quad (CH_3)_3CH \text{ or } \textit{iso}.$$

From the *n* we can get—



$$CH_3\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH \quad \text{and} \quad CH_3\cdot CH_2\cdot CH(OH)\cdot CH_3;$$

from the *iso*—



$$(CH_3)_2CH\cdot CH_2\cdot OH \quad \text{and} \quad (CH_3)_3C\cdot OH;$$

but no more.

Of these isomerides, some only are oxidizable to acids, $C_nH_{2n}O_2$, containing an equal number of carbon atoms, an aldehyde, $C_nH_{2n}O$, being formed as intermediate product. Such alcohols are termed **primary** alcohols (primary propyl, butyl, and isobutyl alcohols, &c.).

Another class of alcohols is not oxidizable to acids with an equal number of atoms of carbon, but to ketones, $C_nH_{2n}O$, by the removal of 2 atoms of hydrogen, *e.g.* isopropyl alcohol yields acetone, C_3H_6O. These are termed **secondary** (secondary butyl alcohol). Upon further oxidation the ketones do indeed yield acids, which, however, contain not an equal but always a smaller number of carbon atoms, the carbon chain having thus been broken up.

Lastly, the third class of alcohols, the **tertiary**, yield upon oxidation neither aldehydes, ketones, nor acids with an *equal* always a smaller number of carbon atoms, due to the fission of the carbon chain.

Constitution of the Alcohols.—In the molecule of a monohydric alcohol one of the hydrogen atoms plays a part different from that of the others; thus it is replaceable by metals (K and Na), and by acid radicals, and, together with the oxygen atom, combines with the hydrogen of a halogen hydride to form water, while the other hydrogen atoms of the alcohol remain unchanged. This hydrogen atom, which has already been formulated under the Theory of Types apart from the others, is called the "typical" or "extra-radical" hydrogen atom. It is not joined directly to the carbon atom, but through the oxygen one, a conclusion which is confirmed by

the formation of alcohols by the action of alkalis (KOH) on monohalogen derivatives of the paraffins. (See p. 74.) This point has been previously discussed (p. 17) for ethyl alcohol.

The alcohols therefore contain a hydroxyl group, OH, and their general constitutional formula is $(C_nH_{2n+1})\cdot OH$.

According to theory, this hydroxyl can either replace an atom of hydrogen in a methyl group, in which case an alcohol containing the group $\cdot CH_2OH$ (one carbon atom being joined to the other by a single bond) results, *e.g.* $CH_3\cdot CH_2\cdot OH$., Or it can replace the hydrogen of a CH_2: group in a hydrocarbon, so that the resulting compound contains the group $:CH\cdot OH$, the carbon being here joined to two other carbon atoms. Or, lastly, it is possible that in a hydrocarbon with a branching carbon chain, the hydrogen of a methine group $CH\vdots$ may be replaced by hydroxyl, when the resulting alcohol would contain the group $\vdots C\cdot OH$, in which one carbon atom is joined to three others.

Now, it is easy to see that the group $\cdot C\Big\langle{}^{H_2}_{O\cdot H}$ can, by further oxidation, be transformed into $\cdot C\Big\langle{}^{O}_{O\cdot H}$. The latter, which is termed carboxyl, is contained in the acids $C_nH_{2n}O_2$, or $C_{n-1}H_{2n-1}COOH$, which are formed by the oxidation of the primary alcohols. Consequently it is the **primary** alcohols which contain the group $\cdot CH_2\cdot OH$.

The group $:CH\cdot OH$ can likewise be changed into $:C:O$ $\left(\textit{i.e.}\ C\Big\langle{}^{OH}_{OH} - H_2O\right)$, which is the characteristic group of the ketones, by oxidation. A further introduction of O or OH, whereby acids containing the group $\cdot CO\cdot OH$ would ensue, is not possible in this case without a rupture of the carbon chain, since the carbon atom is tetravalent. Since then it is the **secondary** alcohols which upon oxidation yield ketones, and not acids with an equal number of carbon atoms, the group $:CH\cdot OH$ is characteristic of these.

Finally, the group $\vdots C\cdot OH$ already contains the maximum of oxygen which can be combined with a carbon atom already linked to 3 other atoms of carbon. A compound, therefore, in which this atomic group is present, cannot yield, when oxidized, an aldehyde, acid, or ketone with an equal number of carbon atoms in the molecule, but the result of such oxidation must be the breaking of the carbon chain, and the formation of acids or ketones containing a smaller number of carbon

atoms in the molecule. This being the behaviour of **tertiary** alcohols, the group $\vdots C \cdot OH$ is peculiar to them. The existence of the three classes of alcohols finds in this way a thoroughly satisfactory explanation from theory.

Secondary and tertiary alcohols were predicted by *Kolbe* in 1859 from theoretical considerations (A. **113**, 301; **132**, 102).

Among the isomeric alcohols the primary possess the highest, and the tertiary the lowest boiling-points (cf. p. 70). Similar generalizations appear to hold good for other physical properties: specific gravity, specific refractive indices, and capillarity constants. The tertiary have the highest melting-points.

Determination of Constitution.—The determination of the constitution of any special alcohol is based largely on its method of formation and on its products of oxidation. *E.g.* Isopropyl alcohol may be obtained by the reduction of acetone $(CH_3)_2 C:O$, and must therefore have the constitutional formula $(CH_3)_2 \cdot CH \cdot OH$, and not $CH_3 \cdot CH_2 \cdot CH_2 \cdot OH$. This is confirmed by the fact that on oxidation it yields the ketone acetone.

Similarly isobutyl alcohol must be represented as $(CH_3)_2 \cdot CH \cdot CH_2 \cdot OH$, since on oxidation it yields *iso*-butyric acid, the constitution of which is known to be $(CH_3)_2 \cdot CH \cdot CO \cdot OH$.

A method of distinguishing primary, secondary, and tertiary alcohols is given on p. 100. Another method suggested is the action of dry potassium hydroxide at 230°. Primary alcohols give acids containing the same number of carbon atoms, secondary yield complex alcohols by condensation, and tertiary are unaffected (*Guerbet*, C.R., 1912, **154**, 222, 713, 1487).

Occurrence.—Different alcohols are found in nature free or combined with organic acids as esters in ethereal oils and waxes.

I. General Methods of Formation.—1. By "**saponification**" or "**hydrolysis**" of their esters, *i.e.* by boiling these with alkalis or mineral acids, or by the action of superheated steam, thus:—

$$\underset{\text{Ethyl benzoate}}{C_6H_5 \cdot CO \cdot OC_2H_5} + KOH = \underset{\text{Potassium benzoate.}}{C_6H_5 \cdot CO \cdot OK} + C_2H_5OH.$$

Some esters, *e.g.* ethyl hydrogen sulphate, decompose when simply warmed with water:

$$C_2H_5 \cdot O \cdot SO_2 \cdot OH + H \cdot OH = C_2H_5 \cdot OH + SO_2(OH)_2.$$

Most of these processes of hydrolysing require some little time, and the ester is boiled with the alkali (KOH solution) in a flask fitted with a reflux condenser.

2. From the halogen compounds $C_nH_{2n+1}X$, and therefore indirectly from the paraffins and olefines (pp. 58 and 60). In the latter case secondary or tertiary alcohols, from C_3 on, are obtained since the halogen of the haloid compounds becomes attached to that carbon atom to which the smaller number of hydrogen atoms are united.

(*a*) By warming these, especially the iodides, with excess of water to 100°; sometimes by simply allowing the mixture to stand (tertiary iodides):



$$C_2H_5I + H.OH = C_2H_5\cdot OH + HI.$$

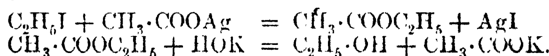
When but little water is used, a state of equilibrium is reached as the reaction is reversible. These halogen compounds may also be termed the esters of the halogen hydracids, so that, strictly speaking, the mode of formation 2*a* is included in 1.

(*b*) Frequently by digesting with moist silver oxide (which acts here like the unknown hydroxide, AgOH), or by boiling with lead oxide and water:



$$C_2H_5I + Ag\cdot OH = C_2H_5\cdot OH + AgI.$$

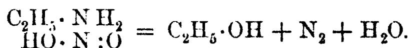
(*c*) Upon warming with silver or potassium acetate, the acetate of the alcohol in question is formed, and this is then hydrolysed:



$$C_2H_5I + CH_3\cdot COOAg = CH_3\cdot COOC_2H_5 + AgI$$
$$CH_3\cdot COOC_2H_5 + HOK = C_2H_5\cdot OH + CH_3\cdot COOK.$$

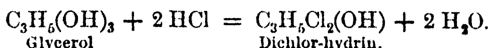
3. By the fermentation of the carbohydrates (*e.g.* grape-sugar), the alcohols with 2, 3, 4, 5, and, under certain conditions, even 6 atoms of carbon are produced. (Yeast fermentation.)

4. On treating the primary amines (see these) with nitrous acid:

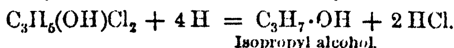


$$\begin{matrix} C_2H_5\cdot NH_2 \\ HO\cdot N:O \end{matrix} = C_2H_5\cdot OH + N_2 + H_2O.$$

5. From polyhydric alcohols by replacing several of the hydroxyl groups by halogen atoms, and then reducing the halogen derivative:



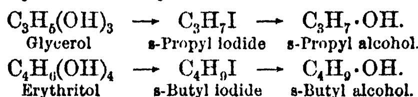
$$C_3H_5(OH)_3 + 2\,HCl = C_3H_5Cl_2(OH) + 2\,H_2O.$$
Glycerol — Dichlor-hydrin.



$$C_3H_5(OH)Cl_2 + 4\,H = C_3H_7\cdot OH + 2\,HCl.$$
Isopropyl alcohol.

Secondary alkyl iodides are often obtained by the action

of HI and P on polyhydric alcohols, and these on hydrolysis yield secondary alcohols, *e.g.*:



$$C_3H_5(OH)_3 \rightarrow C_3H_7I \rightarrow C_3H_7 \cdot OH.$$

Glycerol — s-Propyl iodide — s-Propyl alcohol.

$$C_4H_6(OH)_4 \rightarrow C_4H_9I \rightarrow C_4H_9 \cdot OH.$$

Erythritol — s-Butyl iodide — s-Butyl alcohol.

II. Special Methods of Formation.—1. **Primary alcohols** are obtained from aldehydes by reduction with sodium amalgam and very dilute sulphuric acid (*Wurtz*); or with acetic acid and zinc dust, when the alkyl acetates are formed:

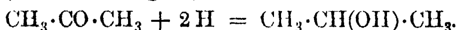


$$CH_3 \cdot CH{:}O + 2H = CH_3 \cdot CH_2 \cdot OH.$$

This reaction is somewhat similar to the reduction of an olefine to a paraffin. In both cases a double bond is converted into a single bond, and an atom of hydrogen is added on to each atom between which the double bond originally existed.

Similarly **from acid anhydrides** (or esters, but not the free acids) and nascent hydrogen, or by the reduction of the acid chlorides, when an ester of the alcohol is formed by the action of the unreduced chloride on the alcohol.

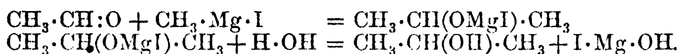
2. **Secondary alcohols** are formed by the action of nascent hydrogen (sodium amalgam) on the ketones, $C_nH_{2n}O$:



$$CH_3 \cdot CO \cdot CH_3 + 2H = CH_3 \cdot CH(OH) \cdot CH_3.$$

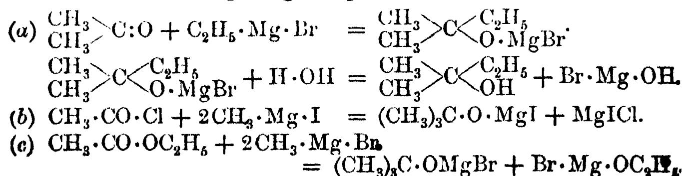
Pinacones are obtained here as by-products. (See Ketones.)

3. **Secondary alcohols** are also formed by the action of aldehydes on dry ethereal solutions of magnesium alkyl halides (p. 124), and treating the product which results with water or dilute acid:



$$CH_3 \cdot CH{:}O + CH_3 \cdot Mg \cdot I = CH_3 \cdot CH(OMgI) \cdot CH_3$$
$$CH_3 \cdot CH(OMgI) \cdot CH_3 + H \cdot OH = CH_3 \cdot CH(OH) \cdot CH_3 + I \cdot Mg \cdot OH.$$

4. **Tertiary alcohols** are formed by the action of (*a*) ketones, (*b*) acid chlorides, or (*c*) esters of organic acids, on magnesium alkyl halides (*Grignard reagents*, pp. 124-7, Ann. Chim. 1901, **24**, 433), and decomposing the products with water:



(*a*) $$\frac{CH_3}{CH_3}{>}C{:}O + C_2H_5 \cdot Mg \cdot Br = \frac{CH_3}{CH_3}{>}C{<}\frac{C_2H_5}{O \cdot MgBr}.$$

$$\frac{CH_3}{CH_3}{>}C{<}\frac{C_2H_5}{O \cdot MgBr} + H \cdot OH = \frac{CH_3}{CH_3}{>}C{<}\frac{C_2H_5}{OH} + Br \cdot Mg \cdot OH.$$

(*b*) $$CH_3 \cdot CO \cdot Cl + 2CH_3 \cdot Mg \cdot I = (CH_3)_3C \cdot O \cdot MgI + MgICl.$$

(*c*) $$CH_3 \cdot CO \cdot OC_2H_5 + 2CH_3 \cdot Mg \cdot Br = (CH_3)_3C \cdot OMgBr + Br \cdot Mg \cdot OC_2H_5.$$

In (*b*) and (*c*) addition of CH_3 and MgBr(I) to the C:O group occurs just as in (*a*), but at the same time a Cl atom in (*b*) and an·OEt group in (*c*) become replaced by CH_3. These methods are a great improvement on the older method of acting on acid chlorides with zinc alkyls (*Butleroff*).

5. **Secondary** or **tertiary alcohols** sometimes ensue by the direct combination of an olefine with water, *e.g.* tertiary butyl alcohol, $(CH_3)_3C\cdot OH$, from isobutylene. This often gives a simple method for converting a primary into a secondary or tertiary alcohol.

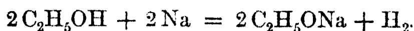
The *Nomenclature* of the alcohols, especially of the secondary and tertiary, is based upon a comparison of them with methyl alcohol, also called carbinol. They are looked upon as carbinol, $CH_3\cdot OH$, in which the three hydrogen atoms are wholly or partially replaced by alkyl radicals, thus:—

Tertiary butyl alcohol, $(CH_3)_3C\cdot OH$ = trimethyl carbinol:
Secondary butyl alcohol, $CH_3\cdot CH_2\cdot CH(OH)\cdot CH_3$,
= $CH(OH)(CH_3)(C_2H_5)$, = methyl-ethyl carbinol

The systematic name of the alcohols terminates in "ol" As examples:—

$CH_3\cdot CH_2\cdot CH_2\cdot CH_2\cdot OH$ Butanol.
$\genfrac{}{}{0pt}{}{CH_3}{CH_3}\!\!>\!CH\cdot CH(CH_3)\cdot CH(OH)\cdot CH_3$ 2:3-Dimethylpentan-4-ol.

Behaviour.—1. The typical hydrogen atom (p. 71) is replaceable by metals, *e.g.* readily by K or Na, less readily by Ca, Mg, or Al with formation of alcoholates, EtONa, $Mg(OEt)_2$, &c.:



$$2\,C_2H_5OH + 2\,Na = 2\,C_2H_5ONa + H_2.$$

These react with water, giving rise to a state of equilibrium as represented in the equation



$$Et\cdot ONa + H\cdot OH \rightleftharpoons Et\cdot OH + Na\cdot OH.$$

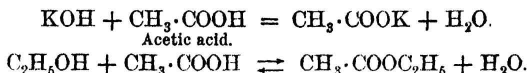
Brühl (B. 1904, **37**, 2066) has described a method for preparing the compound $CH_3\cdot ONa$ free from water and alcohol.

Primary and secondary, but not tertiary, alcohols combine with baryta and lime to alcoholates at 130°. Crystalline compounds are formed with calcium chloride, so that this salt cannot be used for drying the alcohols; these compounds are decomposed by water.

2. They enter into the composition of many compounds, as "alcohol of crystallization". (See pp. 78 and 82.)

3. They react with acids both mineral and organic in some-

what the same manner as metallic hydroxides do, yielding alkyl salts or esters and water (cf. Esterification):



$$KOH + CH_3{\cdot}COOH = CH_3{\cdot}COOK + H_2O.$$
Acetic acid.
$$C_2H_5OH + CH_3{\cdot}COOH \rightleftarrows CH_3{\cdot}COOC_2H_5 + H_2O.$$

The methyl and ethyl esters derived from certain substituted benzoic acids, *e.g.* paranitrobenzoic acid, $NO_2{\cdot}C_6H_4{\cdot}CO_2H$, are solids with definite melting-points, and are sometimes used in identifying small amounts of these alcohols.

4. Dehydrating agents convert them into olefines.

5. With halogen hydracids or phosphorus halides, they yield monohalide derivatives of the hydrocarbons (p. 61).

6. For the behaviour of primary, secondary, and tertiary alcohols upon oxidation, see p. 71 *et seq.*

Methyl alcohol is oxidized to carbon dioxide as the primary product (formic acid) is itself readily oxidized.

7. The primary, secondary, and tertiary alcohols can also be distinguished from one another by the behaviour of the nitro-compounds, which are formed by the action of silver nitrite on the iodides (cf. *Meyer* and *Jacobson*, I, p. 221).

8. Halogens do not substitute but oxidize.

9. Many alcohols when heated with excess of soda lime yield the sodium salts of the corresponding acids.

Methyl alcohol, Methanol, *Wood Spirit*, CH_3OH, was discovered in wood-tar by *Boyle* in 1661, and its difference from ordinary alcohol recognized in 1812 by *Phillips Taylor*. Its composition was established in 1834 by *Dumas* and *Péligot*. It occurs as methyl salicylate in *Gaultheria procumbens* (oil of winter green, Canada), as butyric ester in the unripe seeds of *Heracleum giganteum*, and as ester of benzoylecgonin in cocain

Formation.—1. By chlorinating methane, CH_4, and hydrolysing the resulting methyl chloride (*Berthelot*).

2. By passing $CO + H_2$ over a suitable catalyst (Chap. XLIV).

3. By the destructive distillation of wood (beech, birch, or oak wood) at about 350°. By this distillation there are obtained (*a*) Gases (CH_4, C_2H_6, C_2H_4, C_2H_2, C_3H_6, C_4H_8, CO, CO_2, H_2). (*b*) An aqueous distillate of "pyroligneous acid", containing methyl alcohol (1–2 per cent), acetic acid (10 per cent), acetone (0·1–0·5 per cent), methyl acetate, allyl alcohol, &c. (*c*) Wood-tar, containing paraffins, naphthalene, phenol, guaiacols, &c. (*d*) Wood charcoal.

4. Also by the dry distillation of vinasse.

It is prepared commercially from crude pyroligneous acid by repeated distillation after neutralization with lime, and is purified by formation of the $CaCl_2$ compound, which is a solid, and stable at 100°; or, better, by transformation into the oxalic or benzoic ester, both of which are easy to purify and hydrolyse. At the present time it is largely manufactured by process 2.

Properties.—It is a colourless liquid, boils at 66°, and has a specific gravity about 0·8. The alcohol of commerce usually contains acetone. It burns with a non-luminous flame, dissolves fats, oils, &c., and acts as an intoxicant like ethyl alcohol. It also enters into the composition of compounds as "alcohol of crystallization", *e.g.* $BaO + 2\,CH_4O$; $MgCl_2 + 6\,CH_4O$; $CaCl_2 + 4\,CH_4O$ (six-sided plates). It is readily oxidized to formic aldehyde and formic acid, being also converted into the latter when heated with soda-lime. Potassium methoxide, CH_3OK, is a white crystalline powder, and forms a definite crystalline compound $CH_3OK + CH_3OH$.

The anhydrous alcohol dissolves a small amount of dehydrated cupric sulphate to a blue-green solution. Distilled over heated zinc dust, it decomposes almost quantitatively into $CO + 2\,H_2$.

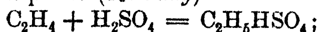
Uses.—For tar colours—(also as CH_3I and CH_3Cl); as methyl ether in the manufacture of ice; for polishes and varnishes; as *Wiggersheim's* preservative liquid; for methylating or "denaturing" spirits of wine, &c.

Ethyl alcohol, Ethanol, *Spirits of Wine*, C_2H_5OH. Liquids containing spirits of wine have been known from very early times, and their concentration either by distillation or by dehydration with carbonate of potash is also an old art. We read of it as "alcohol" in the sixteenth century. *Lavoisier* arrived at the qualitative, and *de Saussure* in 1808 the quantitative composition of alcohol.

In the vegetable kingdom alcohol is only found occasionally, as ethyl butyrate, but in the animal kingdom it occurs in various forms, *e.g.* in diabetic urine. It is also present in small quantity in coal-tar, bone oil, wood spirit, and bread, fresh English bread containing 0·3 per cent.

Formation.—1. From C_2H_6 by conversion into C_2H_5Cl and hydrolysis of the latter, cf. methods of formation 1 and 2.

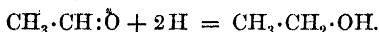
2. Ethylene and concentrated H_2SO_4 react at 160°, yielding ethyl hydrogen sulphate (*Faraday*)



$$C_2H_4 + H_2SO_4 = C_2H_5HSO_4;$$

and this when boiled with water gives ethyl alcohol (cf. p. 73).

3. By the reduction of acetaldehyde, *e.g.* the commercial method of passing aldehyde vapour (from acetylene) and hydrogen over finely divided Ni at 140°.

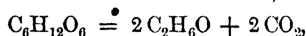


$$CH_3\cdot CH:O + 2H = CH_3\cdot CH_2\cdot OH.$$

4. *Preparation by the Alcoholic Fermentation of Sugar.*—Directly from grape and fruit sugars, $C_6H_{12}O_6$, and indirectly from cane sugar, $C_{12}H_{22}O_{11}$, after previous hydrolysis to two molecules of $C_6H_{12}O_6$; also indirectly from malt-sugar, from starch, &c.

Fermentations are peculiarly slow decomposition-processes of organic substances which are accompanied, as a rule, with liberation of gas and evolution of heat, and which are induced by micro-organisms, or by complex organic nitrogenous substances (*enzymes*) of animal or vegetable origin. The alcoholic fermentation of sugar, *i.e.* the fermentation which produces spirit, is caused by the varieties of the genus *Saccharomyces*, the *yeast ferment*, which forms small oval microscopic cells, multiplying by gemmation. As plants, these require for their sustenance inorganic salts, *e.g.* phosphates, potassium salts, and nitrogen in the form of ammonium salts, but, as non-assimilating fungi, no carbon dioxide.

In the vinous fermentation 94 to 95 per cent of the sugar breaks up into alcohol and carbon dioxide,



$$C_6H_{12}O_6 = 2C_2H_6O + 2CO_2,$$

with 2·5 to 3·6 per cent glycerol, $C_3H_5(OH)_3$, and 0·4 to 0·7 per cent succinic acid, $C_4H_6O_4$, as invariable by-products. In addition to these, most of the higher homologues of ethyl alcohol are also formed—the so-called *fusel oil*—the latter resulting largely from the presence of foreign micro-organisms.

The chief constituent of fusel oil is fermentation amyl alcohol (isobutyl carbinol), $C_5H_{11}OH$, but it has also been proved to contain the two propyl alcohols (chiefly isopropyl), normal, iso, and tertiary butyl alcohols, normal and active amyl alcohols, together with higher homologues and esters. They can be separated by means of their hydrobromic esters.

Conditions of Fermentation.—Fermentation can only go on between the limits of 3° and 35°, the most favourable temperature being between 25° and 30°. The solution must not be too concentrated, as the organism cannot live in a solution of alcohol of greater concentration than 14 per cent; the presence of air is not strictly necessary, but it has a favouring influence.

Yeast loses its activity upon the addition of any reagents which destroy the cells, also when it is thoroughly dried, when heated to 60°, when treated with alcohol, acids, and alkalis; the addition of small quantities of salicylic acid, phenol, corrosive sublimate, &c., also prevents fermentation.

For a number of years it was thought that the presence of the living yeast plant, or of some other similar organism, was essential for the production of alcoholic fermentation. The recent work of *E. Buchner* (B. 1897, **32**, 2086, 2372; 1898, **33**, 971, 2764) has shown that the fermentation is brought about by an enzyme called *Zymase*, which is contained in the cell. If the yeast cells are crushed with "Kieselgühr" (a siliceous earth) and water, so that the cell walls are broken, and the mass then filtered through a Chamberland filter under considerable pressure, an extract is obtained which, although practically free from yeast cells, can yet induce alcoholic fermentation. The zymase is relatively unstable and easily decomposed, *e.g.* when the solution is heated or even kept for some time, but it may be preserved by the addition of certain antiseptic substances, such as chloroform, thymol, &c., which readily kill the yeast plant itself. (Compare Chap. XLVIII.)

Buchner's researches indicate that fermentations induced by organized ferments are probably due to certain unorganized ferments (enzymes) contained in the cells of the organism.

The following materials are used for the preparation of alcohol or of liquids containing alcohol:—

(*a*) Grape-sugar, fruit-sugar, *i.e.* grapes and other ripe fruits, for wine, &c. (*b*) Cane or beet sugar and molasses for brandy. Solutions of cane-sugar are fermented by yeast, since ordinary yeast always contains small amounts of an enzyme (*invertase*), which can hydrolyse cane-sugar to glucose and fructose (cf. p. 326), and these are then directly fermented by the yeast organism. (*c*) The starch of cereals for beer and corn brandy, and of potatoes for potato brandy. The starch is first converted into malt-sugar and dextrine under the influence of diastase, or into grape-sugar, by boiling with dilute acids, and these sugars are then fermented. (*d*) Wood or straw, i.e. cellulose (p. 333), by acid hydrolysis in the presence of a catalyst and subsequent fermentation of the glucose so formed.

The transformation of starch into malt-sugar (maltose) and dextrine is a typical example of fermentation by an *enzyme*, the special enzyme in this case being *diastase*, a complex organic nitrogen derivative produced during the germination of the

barley in the process of malting. The transformation of the starch into maltose, &c., is in reality a process of hydrolysis induced by the ferment. The maltose $C_{12}H_{22}O_{11}$ in its turn is hydrolysed by a second ferment (*maltase*) to grape-sugar $C_6H_{12}O_6$, which is then transformed into alcohol and carbon dioxide.

A wine of medium strength contains 8½ to 10 per cent alcohol, port wine 15 per cent, sherry up to 21 per cent, champagne 8 to 9 per cent, and beer an average of 2 to 6 per cent.

The different varieties of brandy or spirits obtained by "burning", *i.e.* by distilling fermented liquids, contain 30 to 40 per cent alcohol, and cognac even over 50 per cent.

Purification of alcohol. It is difficult to separate alcohol completely from water by distillation, since their boiling-points are only 22° apart from one another. Even after repeated rectification the distillates are found to contain water. The same reason applies to the difficulty of separating alcohol from its higher homologues (fusel oil). From an alcohol containing 30 per cent of water the fusel oil can be extracted by chloroform.

On the large scale this separation is excellently effected by the use of dephlegmators or fractionating columns, which are based upon the principle of partial volatilization and partial cooling of the vapours (*Adam* and *Berard*; improved by *Savalle*, *Pistorius*, *Coffey*, and others). In this way an alcohol containing 98 to 99 per cent can be obtained.

Aqueous alcohol can be deprived of the greater part of its water by the addition of strongly heated carbonate of potash or anhydrous copper sulphate, or by distillation over quicklime, and the last portions can be extracted by baryta, or by several additions of metallic calcium and repeated distillation. Alcohol containing water becomes turbid on being mixed with benzene, carbon bisulphide, or liquid paraffin oil, and it gives a white precipitate of $Ba(OH)_2$ on the addition of a solution of BaO in absolute alcohol, and is capable of restoring the blue colour to anhydrous copper sulphate. Alcohol free from water is termed *absolute* alcohol. Ordinary absolute alcohol usually contains at least 0·2 per cent of water.

Contraction takes place on mixing alcohol and water together, 53·9 volumes alcohol + 49·8 volumes water giving, not 103·7, but 100 volumes of the mixture. The percentage of alcohol in any spirit is determined either from its specific

gravity by reference to a specially-calculated table, or by areometers of particular construction, or by its vapour tension as estimated by *Geissler's* vaporimeter.

Properties.—It is a colourless mobile liquid with characteristic spirituous odour; boils at 78·3°, or at 13° under 21 mm. mercury pressure. Solidifies at −112·3°, and has sp. gr. 0·79 at 15°. It burns with an almost non-luminous flame, is exceedingly hygroscopic, and miscible with water and with ether in all proportions. Forms several cryo-hydrates with water (+12 Aq., +3 Aq., +$\frac{1}{3}$ Aq.). Is an excellent solvent for many organic substances such as resins and oils, and also dissolves sulphur, phosphorus, &c., to some extent. With concentrated sulphuric acid it yields, according to the conditions, ethyl hydrogen sulphate, ether, or ethylene. It diffuses through porous membranes into a dry atmosphere more slowly than water, and coagulates albumen, being therefore used for preserving anatomical preparations.

It is very readily oxidized by the oxygen of the air, either in presence of finely-divided platinum or in dilute solutions in presence of certain ferments, first to aldehyde and then to acetic acid; thus, beer and wine become sour, but not the pure alcohol itself. $K_2Cr_2O_7$ or $MnO_2 + H_2SO_4$ oxidize it in the first instance to aldehyde; fuming nitric acid attacks it with explosive violence, yielding numerous products; but, by the action of colourless concentrated HNO_3, ethyl nitrate can be obtained under suitable conditions; in dilute solution glycollic acid is formed. Alkalis also induce a gradual oxidation in the air; thus, alcoholic potash or soda solutions quickly become brown with formation of aldehyde resin, this latter resulting from the action of the alkali upon the aldehyde first produced. Alcoholic potash therefore frequently acts as a reducing agent, *e.g.* upon aromatic nitro-compounds. (See these.) Chlorine and bromine first oxidize alcohol to aldehyde and then act as substituents. (See Chloral.) Chlorinated alcohols can therefore only be prepared indirectly (cf. Ethylene chlorhydrin). When the vapour of alcohol is led through a red-hot tube, H, CH_4, C_2H_4, C_2H_2, C_2H_6, $C_{10}H_8$, CO, C_2H_4O, $C_2H_4O_2$, &c., are formed.

Of the compounds containing alcohol of crystallization may be mentioned, $KOH + 2\,C_2H_6O$, $LiCl + 4\,C_2H_6O$, $CaCl_2 + 4\,C_2H_6O$, and $MgCl_2 + 6\,C_2H_6O$.

Sodium ethoxide, C_2H_5ONa, is of special importance among the alcoholates. It is formed by the action of sodium upon

absolute alcohol. The crystals of $C_2H_5 \cdot ONa + 2\ C_2H_6O$, at first obtained, lose their alcohol of crystallization at 200° and change into a white powder of C_2H_5ONa. (See also *Brühl*). Sodium ethoxide is of especial value for syntheses, and can frequently be employed in alcoholic solution. This compound, sodium ethylate, or, better, sodium ethoxide is closely related to sodium hydroxide, NaOH.

Small doses of alcohol act as a stimulant, and larger doses as an intoxicant. Absolute alcohol is poisonous, and quickly causes death when injected into the veins. The presence of considerable amounts of fusel oil has detrimental physiological effects.

Detection of Alcohol.—1. By the iodoform reaction * (see Iodoform), when 1 part in 2000 of water can be recognized.

2. By means of benzoyl chloride, C_6H_5COCl, which yields with alcohol the characteristically smelling ethyl benzoate; or of *p*-nitrobenzoyl chloride, which yields ethyl *p*-nitrobenzoate melting at 57°; the corresponding methyl ester melts at 97°.

Propyl alcohols, C_3H_7OH.

1. **Normal propyl alcohol,** 1-*Propanol*, $CH_3 \cdot CH_2 \cdot CH_2 \cdot OH$ (*Chancel*, 1853), is obtained from fusel oil by means of its hydrobromic ester (*Fittig*), or directly by fractionation. It has also been obtained from propionic aldehyde and propionic anhydride by reduction with sodium amalgam (*Rossi*). It is a liquid with a pleasant spirituous odour, and boils 19° higher than ethyl alcohol. It is miscible with water in all proportions, but may be salted out on addition of calcium chloride. Its *constitution* follows from that of propionic acid, into which it is converted on oxidation.

Of the higher alcohols, *n*-**butyl alcohol,** $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot OH$, may be obtained from the fusel oil formed when certain special species of yeast (*Saccharomyces ellipsoidius*) are used in the alcoholic fermentation. This alcohol (25 per cent), acetone (11 per cent), and hydrogen are made on the large scale by the fermentation of maize mash with a special bacterium, and the alcohol is used for synthetic work and for making butyl acetate, a nitrocellulose solvent.

Isobutyl carbinol, $(CH_3)_2{:}CH \cdot CH_2 \cdot CH_2 \cdot OH$, is the chief constituent of the "fermentation amyl alcohol" obtained by fractional distillation of fusel oil, the other constituent being secondary butyl carbinol, $C_2H_5 \cdot CH(CH_3) \cdot CH_2 \cdot OH$.

This latter, on account of its action on polarized light, is

* Acetaldehyde, acetone, and isopropyl alcohol also give this reaction, but not methyl alcohol.

generally known as *active* (*i.e.* optically active) amyl alcohol. It is lævo-rotatory, *i.e.* rotates the plane of polarization to the left (cf. active valeric acid), and has $[\alpha]_D - 5{\cdot}9°$ at 20°.

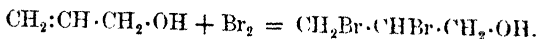
Normal hexadecyl-alcohol, or **cetyl alcohol**, forms as palmitic ester the chief constituent of spermaceti. The cetyl alcohol of commerce contains, in addition, a homologous alcohol, $C_{18}H_{38}O$.

Ceryl alcohol, *Cerotin*, $C_{26}H_{53}OH$, forms as cerotic ester Chinese wax.

Melissic, or **miricyl alcohol**, $C_{30}H_{61}OH$, is present as palmitic ester in bees'-wax and in Carnauba wax (from leaves of Brazilian palm), and is most conveniently prepared from the latter. The alcohols are obtained from all these esters (wax varieties) by hydrolysis with boiling alcoholic potash.

B. Monohydric Unsaturated Alcohols, $C_nH_{2n-1}OH$

These are very similar to the saturated alcohols both in physical properties and in general chemical behaviour, but are sharply distinguished from the latter by the formation of additive compounds with hydrogen, halogens, halogen hydracids, &c., *e.g.*:



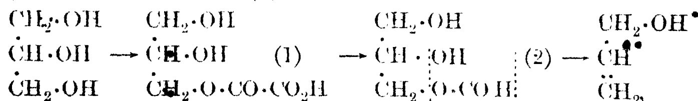
$$CH_2{:}CH{\cdot}CH_2{\cdot}OH + Br_2 = CH_2Br{\cdot}CHBr{\cdot}CH_2{\cdot}OH.$$

They thus resemble the olefines owing to the presence of a double bond, and the products are saturated alcohols or their halide derivatives, the latter of which cannot be prepared directly by substitution of the alcohols. These unsaturated alcohols are to be considered as olefines in which an atom of hydrogen is replaced by hydroxyl.

According to theory, the existence of alcohols which contain the hydroxy-methylene group, $:CH(OH)$, linked to a carbon atom by a double bond, might be predicted. To this class belongs **vinyl alcohol** (*ethenol*), $CH_2{:}CH{\cdot}OH$, which occurs in commercial ether, but which has not yet been isolated (B. **22**, 2863), although derivatives of it are known. By the reactions in which one would expect it to be formed, its isomer, $CH_3{\cdot}CHO$ (acetaldehyde), is formed; in fact, the grouping $:C{:}CH{\cdot}OH$ is usually unstable, passing as it does into the more stable one, $:CH{\cdot}CH{:}O$, a transformation which is most readily explained upon the assumption that water is taken up and again split off. Similarly, instead of the group $CH_2{:}C(OH){\cdot}CH_3$, we always get $CH_3{\cdot}CO{\cdot}CH_3$.

Allyl alcohol (*1-Propene-3-ol*), $CH_2:CH\cdot CH_2OH$ (*Cahours* and *Hofmann*, 1856), is present to the extent of 0·1 to 0·2 per cent in wood spirit, and is formed (1) from allyl iodide; (2) by reduction of its aldehyde, acrolein (see this); (3) by heating glycerol, $C_3H_5(OH)_3$, with oxalic or formic acid and a little ammonium chloride to 220°.

Cf. Formic Acid (p. 153). The first product is glyceryl monoxalate (1), which loses CO_2, forming glyceryl monoformate or monoformin (2).



and this when heated to the required temperature, 220°, decomposes into CO_2, H_2O, and allyl alcohol. Allyl alcohol is a mobile liquid of suffocating smell, having almost the same boiling-point (97°) as *n*-propyl alcohol; like the latter, it is miscible with water. It does not take up nascent hydrogen directly, but chlorine, bromine, cyanogen, hypochlorous acid, &c. If cautiously oxidized, it yields glycerol, but stronger oxidation converts it into its aldehyde, acrolein, and acid, acrylic acid, containing the same number of carbon atoms, and it is therefore a primary alcohol; hence the above *constitutional formula.*

C. Monohydric Unsaturated Alcohols, $C_nH_{2n-3}\cdot OH$

These alcohols are derivatives of acetylene and its homologues. The compounds possess:—(1) The characteristic pro perties of alcohols. (2) The properties of unsaturated compounds. Each molecule of such an alcohol can combine with 1 or 2 molecules of a halogen or halogen hydracid. (3) Most of them possess the further peculiarity of forming explosive compounds with ammoniacal copper and silver solutions, *e.g.* C_3H_2AgOH, the former being coloured yellow and the latter white; acids decompose these compounds into the unsaturated alcohol. Those of them which do not yield such metallic compounds contain, not a triple bond, but two double ones between the carbon atoms. The most important of these alcohols is—

Propargyl alcohol, or *propinyl alcohol* (*1-Propin-3-ol*),



$$C_3H_3OH, = CH{:}C\cdot CH_2OH,$$

a mobile liquid of agreeable odour, lighter than water, and boiling at 114°, *i.e.* somewhat higher than normal propyl alcohol.

For further examples of unsaturated alcohols, see Open-chain Terpenes (Chap. XLI, A).

IV. DERIVATIVES OF THE ALCOHOLS

These may be classed in the following divisions:—

A. Ethers of the alcohols, or alkyl oxides, *e.g.* $C_2H_5 \cdot O \cdot C_2H_5$, ethyl ether.

B. Thio-alcohols and ethers, or alkyl hydrosulphides and sulphides, *e.g.* $C_2H_5 \cdot SH$ and $(C_2H_5)_2S$.

C. Nitrogen bases of the alcohol radicals.

D. Other metalloid compounds of the alcohol radicals.

E. Metallic compounds of the alcohol radicals, or organo-metallic compounds.

A. Ethers Proper (Alkyl- or Alphyl-Oxides)

The ethers of the monohydric alcohols are compounds of neutral character derived from the alcohols by elimination of the elements of water (1 molecule water from 2 molecules alcohol). They can frequently be prepared by treating the alcohols with sulphuric acid, and are distinguished from the latter by not reacting with acids to form esters, and by being substituted and not oxidized by the halogens, &c. Only the lowest member of the series is gaseous, most of them are liquid, and the highest are solid. The more volatile ethers are characterized by a peculiar odour which is not shown by the higher members.

Constitution.—The hydrogen atoms cannot be replaced by sodium or other metallic radicals (see p. 18), and are all presumably attached to carbon.

Their structure as alkyl oxides, or anhydrides of monohydric alcohols (cf. metallic oxides), follows largely from modes of formation 2 and 3, from the non-reactive character of the hydrogen atoms, and from reactions 4 and 5, p. 88.



$$\begin{matrix} KOH \\ KOH \end{matrix} = K_2O + H_2O; \quad \begin{matrix} C_2H_5OH \\ C_2H_5OH \end{matrix} = \begin{matrix} C_2H_5 \\ C_2H_5 \end{matrix}\!\!>O + H_2O.$$

The alkyl groups contained in them may either be the same, as in ordinary ether and in methyl ether, $(CH_3)_2O$, in

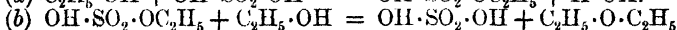
which case they are termed "**simple ethers**"; or they may be different, as in methyl-ethyl ether, $CH_3 \cdot O \cdot C_2H_5$, when they are known as "**mixed ethers**".

Ethers derived from tertiary alcohols are not known.

Modes of Formation.—1. By heating the alcohols, $C_nH_{2n+1} \cdot OH$, with sulphuric acid. The reaction proceeds in two phases, *e.g.*:



(*a*) $C_2H_5 \cdot OH + OH \cdot SO_2 \cdot OH = OH \cdot SO_2 \cdot OC_2H_5 + H \cdot OH.$



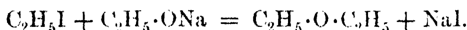
(*b*) $OH \cdot SO_2 \cdot OC_2H_5 + C_2H_5 \cdot OH = OH \cdot SO_2 \cdot OH + C_2H_5 \cdot O \cdot C_2H_5$

In phase *a* an alkyl hydrogen sulphate is formed, which, when further heated with alcohol, as in *b*, yields ether and regenerates sulphuric acid. The latter is therefore free to work anew, and in this way to convert a very large quantity of alcohol into ether.

This process is theoretically a continuous one, but practically it has its limits, through secondary reactions, such as the formation of SO_2, &c. A modification of the method consists in heating the alcohol with benzene-sulphonic acid $C_6H_5 \cdot SO_2 \cdot OH$ in place of sulphuric acid. No sulphur dioxide is formed, and the reaction becomes in reality continuous. The method is only suitable for primary alcohols; secondary and tertiary under similar conditions yield olefines. Hydrochloric, hydrobromic, and hydriodic, among other acids, act similarly to sulphuric acid; thus ether is obtained when alcohol is heated with dilute hydrochloric acid in a sealed tube to 180°, ethyl chloride, C_2H_5Cl, being formed as an intermediate product. When alcohol is heated with hydrochloric acid, a state of equilibrium is established between the alcohol, ether, ethyl chloride, hydrochloric acid, and water, after which the same quantity of each of these products is destroyed as is formed in unit of time.

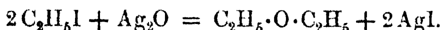
For preparation from alcohols and Al_2O_3 or alum, cf. XLIX, B.

2. By the action of alkyl halides on sodium-alkylate, or also upon alcoholic potash:



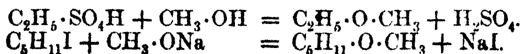
$$C_2H_5I + C_2H_5 \cdot ONa = C_2H_5 \cdot O \cdot C_2H_5 + NaI.$$

3. From alkyl halides and dry silver oxide, or mercuric oxide:



$$2\,C_2H_5I + Ag_2O = C_2H_5 \cdot O \cdot C_2H_5 + 2\,AgI.$$

Modes of formation 1 and 2 yield mixed as well as simple ethers, *e.g.*:

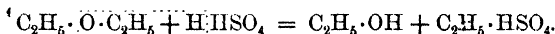


$$C_2H_5 \cdot SO_4H + CH_3 \cdot OH = C_2H_5 \cdot O \cdot CH_3 + H_2SO_4.$$
$$C_5H_{11}I + CH_3 \cdot ONa = C_5H_{11} \cdot O \cdot CH_3 + NaI.$$

Properties.—1. The ethers are very stable, *e.g.* ammonia, alkalis, dilute acids, and metallic sodium have no action upon them, nor has phosphorus pentachloride in the cold.

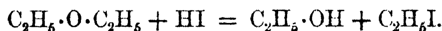
2. When superheated with water in presence of some acid, such as sulphuric, the ethers take up water and are retransformed into alcohols, the secondary more readily than the primary; this change also proceeds, but extremely slowly, at the ordinary temperature.

3. When warmed with concentrated sulphuric acid, alcohol and ethyl hydrogen sulphate are formed:



$$C_2H_5 \cdot O \cdot C_2H_5 + H \cdot HSO_4 = C_2H_5 \cdot OH + C_2H_5 \cdot HSO_4.$$

4. When saturated with hydriodic acid gas at 0°, the ethers yield alcohol and alkyl iodide:



$$C_2H_5 \cdot O \cdot C_2H_5 + HI = C_2H_5 \cdot OH + C_2H_5I.$$

When the ethers are "mixed", the iodine attaches itself to the smaller alkyl group; further interaction yields, of course, two molecules of alkyl iodide.

5. When heated with phosphorus halides the oxygen atom is replaced by two halogen atoms, and two molecules of an alkyl halide are formed.

6. Like the alcohols, the ethers are oxidized by nitric and chromic acids, but halogens substitute in them and do not oxidize; in this latter respect they resemble the hydrocarbons.

7. Many ethers form definite compounds with acids, especially complex acids like $H_4FeC_6N_6$ (B. 1901, **34**, 2688); also with bromine, with metallic salts, &c. (J. C. S. 1904, **85**, 1106; Proc. 1904, 165).

Ethyl ether, Ethane-oxy-ethane, "*Ether*" $(C_2H_5)_2O$, was discovered by *Valerius Cordus* about 1544, and possibly before that time by *Raymond Lully*. It was also called "sulphuric ether", and "vitriol ether", on account of its being supposed to contain sulphur. Its composition was established by *Saussure* in 1807, and *Gay-Lussac* in 1815.

Preparation.—By the continuous process from ethyl alcohol and sulphuric acid at 140°, with gradual addition of the alcohol, according to *Boullay*. It is freed from alcohol by shaking with water, and dried by distillation over lime or calcium chloride, and finally over metallic sodium.

Theories of the Formation of Ether.—At first the action of the sulphuric acid was considered to consist in an abstraction of water. Later on, it was thought that the acid gave rise to

a contact action (*Mitscherlich*, *Berzelius*), but *Liebig* showed that this view was incorrect, since ethyl hydrogen sulphate is formed. *Liebig* assumed that the ethyl hydrogen sulphate decomposed, when heated, into ether and SO_3; but *Graham*, on the other hand, proved that the acid gives no ether when heated alone to 140°, but only when heated along with more alcohol.

After this, *Williamson* propounded the theory of etherification at present held, a theory based on the opinion of *Laurent* and *Gerhardt* that ether contains two ethyl radicals. Its correctness was proved by mode of formation 2, and also by the preparation of mixed ethers.

Properties.—It is a mobile liquid with powerful ethereal odour, and is very volatile, even at the ordinary temperature. It melts at −113°, boils at +34·9°, has specific gravity = 0·72 at 17·4°, and at 120° has a vapour pressure of 10 atmospheres. It produces considerable lowering of temperature when evaporated. It is easily inflammable, and therefore dangerous as a cause of fire, from the dissemination of its very heavy vapour; a mixture of it with oxygen or air is explosive. It is somewhat soluble in water (1 part in 10), and, conversely, 3 volumes of water dissolve in 100 volumes of ether; the presence of water can be detected by the milkiness which ensues upon the addition of carbon disulphide. Ether is an excellent solvent or extractive for many organic substances, and also for I_2, Br_2, CrO_3, $FeCl_3$, $AuCl_3$, $PtCl_4$, and other chlorides. It forms crystalline compounds with various substances, *e.g.* the chlorides and bromides of Sn, Al, P, Sb, and Ti, being present in them as "ether of crystallization".

When dropped upon platinum black it takes fire, and when poured into chlorine gas an explosion results, hydrochloric acid being set free. In the dark, however, and in the cold, substitution by chlorine is possible; the final product of the substitution, perchloro-ether, $C_4Cl_{10}O$, is solid and smells strongly like camphor.

Ether was first employed as an anæsthetic by *Simpson* in 1848, but this property had been previously observed by *Faraday*. It is further used as an extractive in the colour industry, as *Hofmann's* drops when mixed with 1 to 3 volumes of alcohol, for ice machines, and for the preparation of collodion, &c.

Methyl ether, $(CH_3)_2O$ (*Dumas*, *Péligot*), closely resembles common ether, is gaseous at the ordinary temperature, but

liquid under $-20°$, and is prepared on the large scale for the production of artificial cold.

• **Ethyl-cetyl-** and **dicetyl ethers** are solid at the ordinary temperatures.

Several ethers with unsaturated alcohol radicals are also known, *e.g.* **allyl ether**, $(C_3H_5)_2O$, and **vinyl-ethyl ether**, $C_2H_3 \cdot O \cdot C_2H_5$. B.-pt. 35°·5. These can combine directly with bromine.

Isomers.—The general formula of the saturated ethers is $C_nH_{2n+2}O$. Isomeric with each ether is a saturated alcohol, thus C_2H_6O = methyl ether or ethyl alcohol, $C_4H_{10}O$ = diethyl ether or butyl alcohol. From $C_4H_{10}O$ on, however, several different isomeric ethers are not only possible, but are also known, *e.g.* di-ethyl ether, $(C_2H_5)_2O$, is isomeric with methyl-propyl ether, $CH_3 \cdot O \cdot C_3H_7$; similarly methyl-amyl ether, $CH_3 \cdot O \cdot C_5H_{11}$, ethyl-butyl ether, $C_2H_5 \cdot O \cdot C_4H_9$, and dipropyl-ether, $C_3H_7 \cdot O \cdot C_3H_7$, are all isomeric. Isomerism of this kind depends upon the fact that the alkyl radicals—and hydrogen—are homologous, so that if the numbers of carbon atoms are equal, so also must be the numbers of hydrogen.

Such isomerism in which the compounds belong to the same class and differ only in the nature of the alkyl group present is termed **metamerism**.

The determination of the *constitution* of the ethers is based upon (*a*) their syntheses according to modes of formation 1 or 2, and (*b*) their decomposition by HI according to Reaction 4.

Varieties of Isomerism.—The cases of isomerism which have been mentioned up to now are of three kinds. The first was the isomerism of the higher paraffins, which, since it is based upon the dissimilarity of the carbon chains, is often termed **chain-isomerism**. The isomerism between ethylene and ethylidene chlorides or between primary and secondary propyl alcohols depends upon the differences in position of the substituting halogen or hydroxyl in the same carbon chain, and is termed **position isomerism**. In addition to these there is the third kind, **metamerism**. Further cases will be spoken of under the Benzene derivatives.

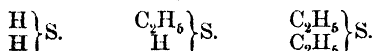
B. Thio-alcohols and -ethers

The relationship between oxygen and sulphur, indicated by their positions in the periodic classification of the elements, is supported by a study of their carbon derivatives. We have

a group of sulphur compounds analogous to the monohydric alcohols. These are known as thio-alcohols or "thiols". Similarly a group corresponding with the ethers is known as the thio-ethers or alkyl sulphides. These are liquids of a most unpleasant and piercing odour, something like that of leeks; they are nearly insoluble in water, and the lower members are very volatile. The higher homologues are not so soluble in water, but continue to be soluble in alcohol and ether, and their smell is less strong on account of the rise in the boiling-point. They are readily inflammable.

The **thio-alcohols**, also called **mercaptans** or **alkyl hydrosulphides**, *e.g.* mercaptan, ethan-thiol, $C_2H_5 \cdot SH$, although of neutral reaction, possess the chemical characters of weak acids and are capable of forming salts, the "mercaptides", especially mercury compounds. The name "mercaptan" is derived from "corpus mercurio aptum". They are soluble in a strong solution of potash, and their boiling-points are distinctly lower than those of the corresponding alcohols. The **thio-ethers**, also termed **alkyl sulphides**, *e.g.* ethyl sulphide, $(C_2H_5)_2S$, are on the other hand neutral volatile liquids without acid character.

Both classes of compounds are derived from hydrogen sulphide by the replacement of either one or both atoms of hydrogen by alkyl groups, just as alcohol and ether are derived from water:



$$\left.\begin{matrix}H\\H\end{matrix}\right\}S. \qquad \left.\begin{matrix}C_2H_5\\H\end{matrix}\right\}S. \qquad \left.\begin{matrix}C_2H_5\\C_2H_5\end{matrix}\right\}S.$$

The boiling-points are methyl mercaptan 6°, ethyl mercaptan 36°, methyl sulphide 37°, ethyl sulphide 92°.

The *constitution* of these compounds follows at once from their modes of formation.

Formation.—The mercaptans may be obtained—

1. By warming an alkyl halide or sulphate with potassium hydrosulphide in concentrated alcoholic or aqueous solution:



$$C_2H_5Br + KSH = C_2H_5 \cdot SH + KBr.$$

2. By heating alcohol with phosphorus pentasulphide, the oxygen being thus replaced by sulphur (*Kekulé*).

The thio-ethers are similarly obtained—

1. From an alkyl halide or potassium alkyl sulphate and normal potassium sulphide:



$$2C_2H_5 \cdot SO_4K + K_2S = (C_2H_5)_2S + 2K_2SO_4.$$

2. By treating ethers with phosphorus pentasulphide.

"Mixed sulphides", comparable with the "mixed ethers", can also be prepared, *e.g.* methyl-ethyl sulphide, $C_2H_5 \cdot S \cdot CH_3$.

Behaviour.—A. **The Mercaptans.**

1. Sodium and potassium act upon the mercaptans to form sodium and potassium salts, white crystalline compounds, which are decomposed by water. The mercury salts are obtained by warming an alcoholic solution of mercaptan with mercuric oxide, *e.g.* **mercuric mercaptide**, $Hg(C_2H_5S)_2$ (white plates). With mercuric chloride sparingly soluble double compounds are formed, *e.g.* $(C_2H_5 \cdot S)Hg \cdot Cl$, a white precipitate. The lead salts are yellow-coloured, and are formed when alcoholic solutions of a mercaptan and of lead acetate are mixed.

2. When oxidized with nitric acid the mercaptans are transformed into **alkyl-sulphonic acids**:



$$C_2H_5 \cdot SH + 3O = {}^{C_2H_5}_{HO}\!\!>\!S\!\!<^{O}_{O} \text{ (ethyl-sulphonic acid).}$$

3. The mercaptans in the form of sodium salts are oxidized by iodine or by sulphuryl chloride, SO_2Cl_2 (B. **18**, 3178), and also frequently in ammoniacal solution in the air to **disulphides**, *e.g.* **ethyl disulphide**, $(C_2H_5)_2S_2$, thus:—



$$2\,C_2H_5S \cdot Na + I_2 = C_2H_5 \cdot S \cdot S \cdot C_2H_5 + 2\,NaI.$$

These are disagreeably-smelling liquids, which have much higher boiling-points than the mercaptans. They are reduced by nascent hydrogen, and with nitric acid yield **disulphoxides**, *e.g.* **ethyl disulphoxide**, $(C_2H_5)_2S_2O_2$.

B. **The Thio-ethers.**—1. They yield additive compounds with metallic salts, *e.g.* $(C_2H_5)_2S$, $HgCl_2$, which can be crystallized from ether.

2. They are capable of combining with halogen or oxygen. Thus ethyl sulphide forms with bromine a **dibromide**, $(C_2H_5)_2S:Br_2$, crystallizing in yellow octohedra, and with dilute nitric acid, **diethyl sulphoxide**, $(C_2H_5)_2S:O$, a thick liquid soluble in water, which combines further with nitric acid to the compound, $(C_2H_5)_2SO$, HNO_3. Concentrated nitric acid or potassic permanganate oxidizes the sulphides or sulphoxides to **sulphones**, *e.g.* ethyl sulphide to **(di)-ethyl sulphone**, $(C_2H_5)_2SO_2$, and methyl-ethyl sulphide to **methyl-ethyl sulphone**, $(CH_3)(C_2H_5)SO_2$. The sulphones are solid well-characterized compounds which boil without decomposition.

The sulphoxides are reduced by nascent hydrogen to sulphides, but not the sulphones.

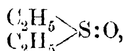
3. The behaviour of the sulphides towards the alkyl halides is of especial interest. Thus the substances $(CH_3)_2S$ and CH_3I combine even in the cold to the white crystalline **trimethyl-sulphine iodide**, $(CH_3)_3SI$, or **trimethyl-sulphonium iodide**, as it is now generally called in order to emphasize its similarity to the ammonium salts; this is soluble in water, and when heated is resolved into its components. It behaves exactly like a salt of hydriodic acid, and yields with moist silver oxide —(but not with alkali)—an oily base, **trimethyl-sulphonium hydroxide**, $(CH_3)_3S \cdot OH$, which cannot be volatilized without decomposition. This is as strong a base as caustic potash, and resembles the latter so closely that it absorbs carbon dioxide, cauterizes the skin, drives out ammonia, and gives salts with acids even with hydrogen sulphide; these latter closely resemble the alkali sulphides, *e.g.* they dissolve Sb_2S_3 (*Oefele*, 1833; *Cahours*).

The compounds just described are of particular interest with regard to the question of the **valency of sulphur**.

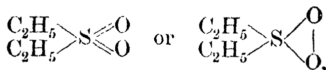
The readiness with which these sulphur compounds are oxidized, and the ease with which they yield additive compounds, is undoubtedly due to the readiness with which the S atom passes from the di- to the tetra- or hexa-valent state.

$\begin{matrix}CH_3\\CH_3\end{matrix}\!>\!S$ with Br_2 gives $\begin{matrix}CH_3\\CH_3\end{matrix}\!>\!S\!<\!\begin{matrix}Br\\Br\end{matrix}$, and with CH_3I, $\begin{matrix}CH_3\\CH_3\end{matrix}\!>\!S\!<\!\begin{matrix}CH_3\\I\end{matrix}$.

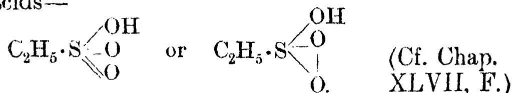
The sulphoxides are—



the sulphones—

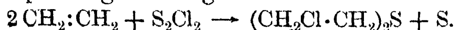


the sulphonic acids—



(Cf. Chap. XLVII, F.)

Mustard gas, or $\beta\beta'$-dichloroethyl sulphide, $(CH_2Cl \cdot CH_2)_2S$, was manufactured in large quantities by the following reaction for use as a poison gas during the war:—



$$2\,CH_2{:}CH_2 + S_2Cl_2 \longrightarrow (CH_2Cl \cdot CH_2)_2S + S.$$

(*Gibson* and *Pope*, J. C. S., 1920, **117**, 271.)

Since in ethyl sulphide both the alkyl radicals are bound to the sulphur, this will also be the case in ethyl sulphone, otherwise the sulphones would manifestly be easily saponifiable. (See Ethyl-hydrogen sulphite.) The sulphonium hydroxides also can only be explained very insufficiently as molecular compounds, on the assumption of the divalence of sulphur. The formula $(CH_3)_2S + CH_3OH$ for trimethylsulphine hydroxide does not indicate in the least the strongly basic character of this substance, since it is not explicable why the mere addition of the neutral methyl alcohol to the equally neutral methyl sulphide should produce such an effect.

With respect to isomers, the same general conditions prevail in the sulphur as in the corresponding oxygen compounds.

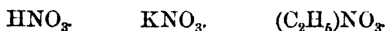
SULPHIDES OF UNSATURATED ALCOHOL RADICALS

Allyl sulphide, $(C_3H_5)_2S$ (*Wertheim*, 1844), present in the oil of *Allium sativum*—oil of garlic,—in *Thlaspi arvense*, &c., may be prepared from allyl iodide and K_2S (*Hofmann*, *Cahours*). B.-pt. 140°.

Analogous **alkyl selenium** and **tellurium compounds** are also known. They are in part distinguished by their excessively disagreeable, nauseous, and persistent odour.

C. Esters of the Alcohols with Inorganic Acids and their Isomers

The esters or alkyl salts may be considered as derived from the acids (see p. 77) by the exchange of the replaceable hydrogen of the latter for alkyl radicals, just as metallic salts result by exchanging the hydrogen for a metallic radical:



$$HNO_3. \qquad KNO_3. \qquad (C_2H_5)NO_3.$$

Or they are derived from the alcohols by exchange of the hydroxyl radical for acid radicals, *e.g.* $C_2H_5{\cdot}NO_3$, ethyl nitrate; $C_2H_5{\cdot}SO_4H$, ethyl hydrogen sulphate; and $C_2H_5{\cdot}Cl$, ethyl chloride.

Monobasic acids yield only one kind of ester, "**neutral or normal esters**", which are analogous to the normal metallic salts of those acids.

Dibasic acids yield two series of esters—(1) **acid esters** and (2) **neutral esters**—corresponding respectively with acid and normal salts; thus, $C_2H_5{\cdot}HSO_4$ and $(C_2H_5)_2{:}SO_4$ are the acid

and normal ethyl esters of sulphuric acid. Tribasic acids yield three series of esters, &c.

The composition of the esters or alkyl salts is therefore exactly analogous to that of metallic salts, so that in the definition of polybasic acids their behaviour in the formation of esters may also be included.

The normal esters are mostly liquids of neutral reaction, and often of very agreeable odour, with relatively low boiling-points, and volatilize, eventually in a vacuum, without decomposition. Most of them are very sparingly soluble in water. The acid esters, also called ester-acids, on the other hand, are of acid reaction, without smell, usually very readily soluble in water, much less stable than the neutral esters, and not volatile without decomposition. They act as acids, *i.e.* form salts and esters.

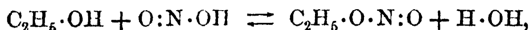
All esters are able to combine with water, and are by this means resolved again into their components, namely, alcohol and acid, *e.g.*—



$$C_2H_5NO_3 + H_2O = C_2H_5OH + HNO_3.$$

This process occurs when the ester is boiled with alkalis or acids, or when heated with steam to over 100°, *e.g.* 150°–180°, and is termed **hydrolysis**, or *saponification*, when alkalis are used (see Soaps, p. 164). The reaction is usually conducted in a flask fitted with a reflux condenser, but in a few cases the reaction takes place when the ester is mixed with water at the ordinary temperature.

General Modes of Formation.—1. The simplest method for obtaining an ester is by the action of the acid on the alcohol, water always being formed as a by-product. As the reactions are reversible,



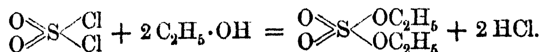
$$C_2H_5\cdot OH + O{:}N\cdot OH \rightleftarrows C_2H_5\cdot O\cdot N{:}O + H\cdot OH,$$

it is essential that the water formed should be removed from the sphere of action by the aid of concentrated sulphuric acid, fused zinc chloride, &c., or that a large excess of acid should be employed, otherwise after a short time a state of chemical equilibrium is reached, all four compounds are present, and the direct and reverse reactions are proceeding at the same rate; even prolonged heating will then not transform any further amounts of acid and alcohol into ester.

Esters are therefore often prepared by adding an excess of

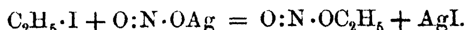
concentrated sulphuric acid to a mixture of the alcohol and sodium salt of the acid.

2. The alcohol is heated with the acid chloride, thus:—



$$O_2S\langle^{Cl}_{Cl} + 2\,C_2H_5\cdot OH = O_2S\langle^{OC_2H_5}_{OC_2H_5} + 2\,HCl.$$

3. The silver salt of the acid is heated with an alkyl iodide; this is a method of very general application, although it often leads to isomers of the expected ester (see also p. 97):



$$C_2H_5\cdot I + O{:}N\cdot OAg = O{:}N\cdot OC_2H_5 + AgI.$$

Besides the true esters, there are also included in this division several other classes of acid derivatives isomeric with them, but distinguished from them by not being readily hydrolysed, *i.e.* by being more stable, *e.g.* nitro-compounds, sulphonic and phosphinic acids, &c. The hydrocyanic derivatives of the alcohols will also be described here for the sake of convenience. These, also, are not hydrolysed in the normal manner into alcohol and acid, but are decomposed in quite a different manner.

ESTERS OF NITRIC ACID

Methyl nitrate, $CH_3\cdot O\cdot NO_2$, is a colourless liquid, boiling at 66°. **Ethyl nitrate**, $C_2H_5\cdot O\cdot NO_2$ (*Millon*), is a mobile liquid of agreeable odour and sweet taste, but with a bitter after-taste; it boils at 86°, and burns with a white flame. Both esters are soluble in water. The latter is prepared directly from the alcohol and acid, with the addition of urea in order to destroy any nitrous acid as fast as it is formed.

Nitric esters contain a large proportion of oxygen in a form in which it is readily given up; they therefore explode when suddenly heated. They are very readily hydrolysed to nitric acid and the alcohol when boiled with alkalis. Tin and hydrochloric acid reduce them to hydroxylamine:



$$C_2H_5\cdot O\cdot N\langle^{O}_{O} + 6\,H = C_2H_5\cdot OH + H_2N\cdot OH + H_2O.$$

These two reactions indicate that the nitrogen atom is not directly united to carbon, as it is so readily removed either as nitric acid or as hydroxylamine.

DERIVATIVES OF NITROUS ACID

The compound $C_2H_5O_2N$ exists in two isomeric forms, represented by the formulæ $C_2H_5 \cdot O \cdot N:O$ and $C_2H_5 \cdot N \leqslant^{O}_{O}$. The former is termed ethyl nitrite, as it is the true ester of nitrous acid, $H \cdot O \cdot N:O$; the isomeride is termed nitro-ethane, as it contains the nitro group $\cdot N \leqslant^{O}_{O}$ attached to carbon.

a. **Alkyl nitrites.**—These are obtained by the action of nitrous fumes (from arsenious oxide and nitric acid), or of sodium nitrite and sulphuric acid, or of copper and nitric acid upon the alcohols. They are neutral liquids of aromatic odour, with very low boiling-points, and are readily hydrolysed to the corresponding alcohol and acid. When reduced they yield the alcohol, ammonia, and water.

Methyl nitrite is a gas; **ethyl nitrite** boils at 18°, has a characteristic odour, and in the impure state, as obtained from alcohol, copper, and nitric acid, is used medicinally under the name of "sweet spirits of nitre".

Amyl nitrite, $C_5H_{11} \cdot O \cdot N:O$, is a pale-yellow liquid boiling at 96°, and is used in medicine; it produces expansion of the blood-vessels and relaxation of the contractile muscles.

β. **The Nitro-derivatives** are colourless liquids of ethereal odour, practically insoluble in water, and boiling at temperatures some 100° higher than their isomers. Like the latter they distil without decomposition, and occasionally explode when quickly heated. They are fundamentally distinguished from the alkyl nitrites by not being readily hydrolysed, and by yielding amino-compounds (see these) on reduction, the nitrogen remaining attached to carbon:

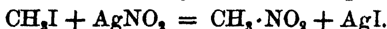


$$CH_3 \cdot N \leqslant^{O}_{O} + 6\,H = CH_3 \cdot NH_2 + 2\,H_2O.$$

Nitro-methane boils at 99°–101°. **Nitro-ethane,** $C_2H_5 \cdot NO_2$ (*V. Meyer* and *Stüber*, 1872), boils at 113°–114°, burns with a bright flame, and the vapour does not explode even at a high temperature.

Formation.—1. The nitro-compounds may be obtained by treating an alkyl iodide with solid silver nitrite (*V. Meyer*). When methyl iodide is used nitro-methane alone is formed, with ethyl iodide about equal weights of nitro-ethane and ethyl nitrite, and the higher homologues in regularly decreas-

ing amounts as compared with those of their isomers, from which, however, they may be readily separated by distillation. Tertiary alkyl iodides do not yield nitro-compounds:

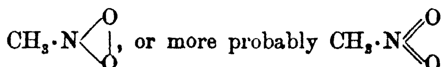


$$CH_3I + AgNO_2 = CH_3{\cdot}NO_2 + AgI.$$

Nitromethane is most readily prepared by the action of sodium nitrite solution on sodium chloroacetate, carbon dioxide being eliminated.

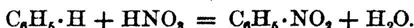
2. The nitro-derivatives of the lower paraffins cannot be obtained by the direct action of nitric acid on the hydrocarbons, but with some of the higher derivatives this is possible, *e.g.* heptane, octane, &c. With decane a 30-per-cent yield of a mono-nitro-derivative may be obtained by means of fuming nitric acid. (*Worstall*, Am. 1898, **20**, 202; 1899, **21**, 211; *Konowaloff*, Abs. 1905, i, 764; 1907, i, 1.) This method is largely employed in the aromatic series (see Nitrobenzene).

The *constitution* of the nitro-compounds is based on the fact that they are not readily hydrolysed, and that the nitrogen is not removed during reduction, but remains directly bound to carbon in the resulting amines (see these). Consequently the nitrogen of the nitro-compound is directly joined to the alkyl radical *i.e.* to carbon; for instance:



Nitrogen which is attached directly to an alkyl radical is therefore not removed by hydrolysing agents. Since the nitrogen of the isomeric alkyl nitrites, on the other hand, is easily split off from the alkyl radical either by hydrolysis or by reduction, it is manifestly not directly combined with the carbon but with the oxygen. The alkyl nitrites, therefore, receive the constitutional formula R·O·N:O, where R represents the alkyl radical.

From this follows for the hypothetical hydrated nitrous acid the formula H·O·N:O, and for the anhydride the formula $(NO)_2O$. The aromatic hydrocarbons, *e.g.* benzene, C_6H_6, yield with nitric acid nitro-compounds, thus:—



$$C_6H_5{\cdot}H + HNO_3 = C_6H_5{\cdot}NO_2 + H_2O.$$

Nitric acid, therefore, contains a nitro-group bound to hydroxyl, corresponding with the formula $H{\cdot}O{\cdot}NO_2$.

Behaviour.—1. They yield primary amines with acid reducing agents, *e.g.* iron and acetic acid, tin and hydrochloric acid,

&c., substituted hydroxylamines being formed as intermediate products (*V. Meyer*, B. 1892, 25, 1714).

2. **Primary** ($\cdot CH_2\cdot NO_2$) and **secondary** ($:CH\cdot NO_2$) nitro-compounds can yield metallic derivatives, and hence possess certain acidic properties. For example, nitro-methane and nitro-ethane react with alcoholic sodium hydroxide, yielding sodium compounds, $CH_2Na\cdot NO_2$ and $CH_3\cdot CHNa\cdot NO_2$. It is almost certain that these sodium salts are not true derivatives of the nitro-compound, but are derived from an isomer, the so-called *iso-nitro*-compound $CH_2:N\genfrac{}{}{0pt}{}{\diagup O}{\diagdown O\cdot H}$, and thus sodium nitro-methane has the constitutional formula $CH_2:NO\cdot ONa$ (*Hollemann*, B. 1900, **33**, 2913). The nitro-derivatives are thus not true acids, but *pseudo acids* (*Hantzsch*, B. 1899, **32**, 577; see also Phenylnitromethane). These sodium salts are crystalline solids, and are highly explosive.

Tertiary nitro-compounds ($:C\cdot NO_2$) contain no hydrogen joined to the carbon atom which is united to the nitro-group, and they have not an acid character; the acidifying influence of the nitro-group does not, therefore, extend to those hydrogen atoms which are attached to other carbon atoms.

The hydrogen in the primary and secondary nitro-derivatives, which is attached to the same carbon atom as the NO_2 group, can also be replaced by bromine. So long as hydrogen, as well as this bromine and the nitro-group, remains joined to the carbon atom in question, the compound is of a strongly acid character; but when it also is substituted by bromine, the compound becomes neutral, *e.g.* dibromo-nitro-ethane, $CH_3\cdot CBr_2\cdot NO_2$, is neutral.

The reactivity of the hydrogen atoms of the $-CH_2\cdot NO_2$ **and** $>CH\cdot NO_2$ **groups, characteristic of primary and secondary nitro-compounds, is exemplified in the reactions of these compounds with aldehydes in the presence of sodium carbonate.** A primary nitro-compound can combine with one or with two molecules of formaldehyde, yielding $-CH(NO_2)CH_2\cdot OH$ and $-C(NO_2)(CH_2\cdot OH)_2$.

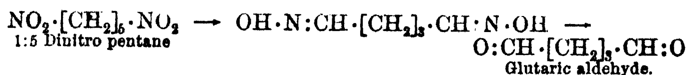
3. The reaction of the nitro-compounds with nitrous acid is very varied. The primary yield **nitrolic acids** and the secondary **pseudo-nitrols**, while the tertiary do not react with it at all. Thus from nitro-ethane, $CH_3\cdot C\genfrac{}{}{0pt}{}{\diagup H_2}{\diagdown NO_2}$, **ethyl-**

nitrolic acid, $CH_3 \cdot C \begin{smallmatrix} \nearrow N \cdot OH \\ \searrow NO_2 \end{smallmatrix}$, an acid crystallizing in light-yellow crystals and yielding intensely red alkali salts, is formed. Normal nitro-propane acts similarly. Secondary nitro-propane, $(CH_3)_2 : CH \cdot NO_2$, gives, on the contrary, **propyl-pseudo-nitrol**, $(CH_3)_2C(NO)(NO_2)$, a white crystalline, indifferent, non-acid substance, which is blue either when fused or when in solution. These reactions, which are only given with compounds of low molecular weight (in the primary up to C_8, and in the secondary up to C_5), are specially applicable for distinguishing between the primary, secondary, or tertiary nature of an alcohol (see p. 77). The nitro-hydrocarbons, which are readily prepared from the iodides, are dissolved in a solution of potash to which sodium nitrite is added, the solution acidified with sulphuric acid and again made alkaline, and then observed for the production of a red coloration (primary alcohol), a blue coloration (secondary alcohol), or no coloration (tertiary alcohol).

Chloropicrin, CCl_3NO_2, a heavy liquid of excessively suffocating smell, b.-pt. 112°, is formed from many hydrocarbon compounds by the simultaneous action of nitric acid and chlorine, chloride of lime, &c. It is best obtained from picric acid and bleaching-powder.

Polynitro-derivatives are also known. **Dinitromethane**, $CH_2(NO_2)_2$, an unstable yellow oil; **dinitroethane**, $CH_3 \cdot CH(NO_2)_2$, obtained from $CH_3 \cdot CHBr \cdot NO_2$ and potassium nitrite, b.-pt. 185°; **trinitromethane** or **nitroform**, $CH(NO_2)_3$, colourless crystals, m.-pt. 15°; **tetranitromethane**, $C(NO_2)_4$, colourless crystals, m.-pt. 13° and b.-pt. 126°, is prepared by the action of nitric acid ($D = 1{\cdot}53$) on acetic anhydride (*Chattaway*, J. C. S. 1910, 2100), or by passing acetylene into nitric acid and a mercury salt, then warming with sulphuric acid and distilling (*Orton*). For constitution, cf. *Schmidt*, B. 1919, 52 B. 400. Good yields (50 per cent) of dinitro-compounds of the type $NO_2 \cdot [CH_2]_n \cdot NO_2$ can be obtained from the corresponding di-iodo-derivatives and silver nitrite (*Von Braun* and *Sobecki*, B. 1911, **44**, 2526) provided $n > 3$. The compounds are stable and react with bromine, nitrous acid, &c., in much the same manner as mono-nitro-compounds. They are accompanied by alkylene dinitrites, $O{:}N \cdot O[CH_2]_n \cdot O \cdot N{:}O$, and nitro-nitrites, $NO_2 \cdot [CH_2]_n \cdot O \cdot N{:}O$, from which they can be separated by fractional distillation. The dinitro-compounds can be used for the preparation of dialdehydes, since when reduced with

stannous chloride they yield dioximes, and these on hydrolysis give dialdehydes:



ESTERS OF SULPHURIC ACID

As a dibasic acid sulphuric acid can give rise to both **neutral** or **normal esters**, *e.g.* $(C_2H_5)_2SO_4$, and **acid esters** or **alkyl hydrogen sulphates**, *e.g.* $C_2H_5HSO_4$.

The neutral esters are formed by the three general methods: (*a*) from fuming sulphuric acid and alcohol; (*b*) from silver sulphate and alkyl iodide; (*c*) from sulphuryl chloride and alcohol: $SO_2Cl_2 + 2\,C_2H_5OH = SO_2(OC_2H_5)_2 + 2\,HCl$.

The acid esters of the primary alcohols are generally prepared directly from their components. Secondary and tertiary alcohols do not yield them.

Ethyl sulphate, $(C_2H_5)_2SO_4$, is a colourless oily liquid of an agreeable peppermint odour, insoluble in water, and solidifying on exposure to a low temperature. It boils at 208°, is quickly hydrolysed with boiling water, but only slowly with cold water, yielding alcohol and sulphuric acid. A 90-per-cent yield is obtained by distilling sodium ethyl sulphate in a vacuum.

Methyl sulphate, $(CH_3)_2SO_4$, is a syrupy oil, b.-pt. 188°, it is extremely poisonous, does not adhere to glass, and is a common reagent used instead of methyl iodide for the formation of methyl derivatives of phenols, alcohols, and amines (cf. S. J., Exp. 127). It is also formed by the direct union of sulphur trioxide and methyl ether (E. P. 1919).

Ethyl hydrogen sulphate, $C_2H_5O \cdot SO_2 \cdot OH$ (*Dabit*, 1802), is obtained from a mixture of alcohol and sulphuric acid, but not quantitatively, on account of the state of equilibrium that ensues. It is also formed from ethylene and sulphuric acid at a somewhat higher temperature. It differs from sulphuric acid by its Ba-, Ca-, and Pb-salts being soluble, and it can therefore be easily separated from the former by means of $BaCO_3$, &c. It yields salts which crystallize beautifully, *e.g.* $KC_2H_5SO_4$, but which slowly decompose into sulphate and alcohol on boiling their concentrated aqueous solution, especially in presence of excess of alkali.

These salts are frequently used instead of ethyl iodide for the preparation of other ethyl derivatives (process of ethylation)

The free acid ester is prepared by adding the requisite amount of sulphuric acid to the barium salt. It is a colourless oily liquid which does not adhere to glass, and which slowly hydrolyses when its solution is evaporated or kept. When heated alone it is decomposed into ethylene and sulphuric acid; with alcohol it yields ethyl ether and sulphuric acid.

DERIVATIVES OF SULPHUROUS ACID

a. **Alkyl Sulphites.**—**Ethyl sulphite,** $SO_3(C_2H_5)_2$, is an ethereal liquid of peppermint odour, which can be prepared from alcohol and thionyl chloride, $SOCl_2$, and which is rapidly hydrolysed by water. It has b.-pt. 161°, and its probable constitution is: $O:S(OEt)_2$.

Ethyl Hydrogen Sulphite.—The very unstable potassium salt, $OEt\cdot SO_2K$, is formed by the action of dry sulphur dioxide on potassium ethoxide (*Rosenheim*, B. 1905, **38**, 1301). It is decomposed by water, yielding alcohol and potassium sulphite.

The action of sodium hydroxide on ethyl sulphite does not hydrolyse the ester to sodium ethyl sulphite, but to sodium ethyl sulphonate, $C_2H_5\cdot SO_2\cdot ONa$. (B. 1898, **31**, 406.)

β. **Sulphonic Acids.**—Sulphonic acids contain the monovalent group $\cdot SO_2\cdot OH$. They are colourless oils or solids, extremely hygroscopic, readily soluble in water, and are strong monobasic acids. They are much more stable than the isomeric alkyl hydrogen sulphites; for example, they are not hydrolysed when boiled with aqueous alkalis or acids, but are decomposed when fused with potash. They are non-volatile with steam, and when strongly heated decompose.

Ethyl-sulphonic acid, $C_2H_5\cdot SO_2\cdot OH$ (*Löwig*, 1839; *H. Kopp*, 1840), is a strong monobasic acid, and yields crystalline salts *e.g.* $C_2H_5\cdot SO_3K + H_2O$ (hygroscopic), $C_2H_5\cdot SO_3Na + H_2O$.

Methyl-sulphonic acid, $CH_3\cdot SO_3H$, is a syrupy liquid, and was prepared by *Kolbe* in 1845 from trichloro-methyl-sulphonic chloride, $CCl_3\cdot SO_2Cl$ (produced from CS_2, Cl, and H_2O).

Modes of Formation.—1. From sodium or ammonium sulphite and alkyl iodide (or alkyl hydrogen sulphate:



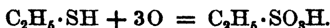
$$C_2H_5\cdot I + Na_2SO_3 = C_2H_5\cdot SO_3Na + NaI.$$

Sulphonic esters are formed by the action of alkyl iodides on silver sulphite:



$$2C_2H_5I + Ag_2SO_3 = (C_2H_5)_2SO_3 + 2AgI.$$

2. **By the oxidation of mercaptans by $KMnO_4$ or HNO_3:**

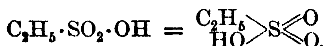


$$C_2H_5{\cdot}SH + 3O = C_2H_5{\cdot}SO_3H.$$

The sulphonic acids yield chlorides with PCl_5, *e.g.* ethyl-sulphonic acid gives **ethyl-sulphonic chloride**, $C_2H_5{\cdot}SO_2Cl$, a liquid which boils without decomposition at 177°, fumes in the air, and is reconverted by water into ethyl-sulphonic and hydrochloric acids. Nascent hydrogen reduces it to mercaptan, and with zinc dust it yields the zinc salt of a syrupy, readily soluble acid, viz. **ethyl-sulphinic acid**, $C_2H_5{\cdot}SO_2H$, which may also be reduced to mercaptan. Sodium ethyl sulphinate yields ethyl sulphone when treated with ethyl bromide, C_2H_5Br. When esterified the acid forms an unstable ester, isomeric with ethyl sulphone (B. **24**, 2272).

Ethyl Ethyl-sulphonate, $C_2H_5{\cdot}SO_2{\cdot}OC_2H_5$, is isomeric with ethyl sulphite, and, being an ester of the more stable ethyl-sulphonic acid, can only be partially hydrolysed. It is prepared from silver sulphite and ethyl iodide. It boils at 213°, and the sulphonic esters generally have considerably higher boiling-points than the isomeric alkyl sulphites.

Constitution.—From the formation of the sulphonic acids from mercaptans by oxidation, and the (indirect) reversibility of this reaction, it follows that the sulphur in them is directly attached to the alkyl radical; if, then, sulphur is regarded as hexavalent, ethyl-sulphonic acid has the constitution



$$C_2H_5{\cdot}SO_2{\cdot}OH = {}^{C_2H_5}_{HO}{>}S{<}^{O}_{O}.$$

This constitution is in perfect harmony with the reaction of the acids with phosphorus pentachloride and also with their monobasicity. From this we might conclude, assuming that the conversion of metallic sulphites into sulphonic acid derivatives is a simple exchange of alkyl and metallic radicals, that the constitution of sodium sulphite is $Na{\cdot}SO_2{\cdot}ONa$, of the hypothetical sulphurous acid $H{\cdot}SO_2{\cdot}OH$, and of sulphuric acid $OH{\cdot}SO_2{\cdot}OH$. The alkyl sulphites formed from thionyl chloride probably have the alkyl groups attached to oxygen, *e.g.* ethyl sulphite, $SO(OC_2H_5)_2$.

Esters of phosphoric acid $PO(OR)_3$, $PO(OR)_2(OH)$, and $PO(OR)(OH)_2$, (R = alkyl), exist, as do also similar compounds of phosphorous and hypophosphorous acids. The phosphinic acids, &c., are related to the two last-mentioned classes. Esters of boric and silicic acids are also known.

ALKYL DERIVATIVES OF HYDROCYANIC ACID

Hydrocyanic acid, HCN, yields two classes of derivatives by the exchange of its hydrogen atom for alkyl radicals, neither of which can be regarded as esters, in the sense that they are hydrolysed to the acid and alcohol.

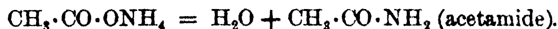
a. **Alkyl Cyanides or Nitriles,** $R \cdot C \vdots N$.—These are either colourless liquids, which volatilize without decomposition, or solids, with an ethereal odour slightly resembling that of leeks; they are lighter than water, and are relatively stable. The lower members are miscible, with water, but the higher ones not, and they boil at about the same temperatures as the corresponding alcohols.

Formation.—1. By heating an alkyl iodide with an alcoholic solution of potassium cyanide, or potassium ethyl-sulphate with potassium ferrocyanide:



$$CH_3I + KCN = KI + CH_3 \cdot CN \text{ (methyl cyanide).}$$

2. From fatty acids, *e.g.* acetic acid, $CH_3 \cdot CO \cdot OH$. The ammonium salt when distilled loses water and yields the acid amide, *e.g.*:



$$CH_3 \cdot CO \cdot ONH_4 = H_2O + CH_3 \cdot CO \cdot NH_2 \text{ (acetamide).}$$

The amide when heated with a dehydrating agent, *e.g.* P_4O_{10}, loses a second molecule of water and yields the cyanide:



$$CH_3 \cdot CO \cdot NH_2 = H_2O + CH_3 \cdot C \vdots N.$$

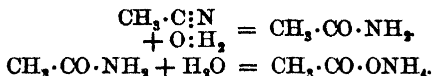
As a consequence of this mode of formation these compounds are also termed **nitriles** of the monobasic acids, *e.g.* $CH_3 \cdot CN$, methyl cyanide or aceto-nitrile; $C_2H_5 \cdot CN$, propionitrile, &c.

3. The higher nitriles, in which $C > 5$, are formed from the amides of acids of the acetic series containing 1 atom of carbon more in the molecule, and also from the primary amines with the same number of carbon atoms, upon treatment with bromine and caustic-soda solution. See Amides, Chap. VII, E.

4. From the oximes of the aldehydes, by warming with acetic anhydride. See Aldoximes, Chap. XLVI, C.

Reactions.—The nitriles are chemically active. Most of the reactions are of an additive nature, and are somewhat similar to those characteristic of the olefines. These reactions are in harmony with the constitutional formulæ usually attributed to the nitriles, *e.g.* $R \cdot C \vdots N$, according to which a triple bond exists between a nitrogen and a carbon atom.

1. When hydrolysed with acids or alkalis, or superheated with water, they take up water (2 mols.) and yield the ammonium salts of fatty acids (with alkalis, the alkali salt, and free ammonia). The reaction undoubtedly proceeds in two distinct stages, and an acid amide is first formed:



$$CH_3{\cdot}C{:}N + O{:}H_2 = CH_3{\cdot}CO{\cdot}NH_2$$
$$CH_3{\cdot}CO{\cdot}NH_2 + H_2O = CH_3{\cdot}CO{\cdot}ONH_4.$$

It is generally impossible to stop the hydrolysis at the first stage in the case of aliphatic nitriles, but this is readily accomplished with aromatic cyanides. This is a reaction of considerable interest, as it enables us to pass from a saturated alcohol, $C_nH_{2n+1}{\cdot}OH$, to the aliphatic acid, $C_nH_{2n+1}{\cdot}COOH$, which contains 1 atom of carbon more than the alcohol:

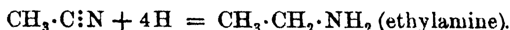


$$CH_3{\cdot}OH \rightarrow CH_3I \rightarrow CH_3{\cdot}CN \rightarrow CH_3{\cdot}COOH.$$

2. Just as acetamide is formed by the taking up of water, so is thio-acetamide by the addition of sulphuretted hydrogen,

3. By the addition of hydrochloric acid, amido-chlorides or imido-chlorides are formed; by the addition of ammonia bases, amidines. Halogens also form decomposable additive-products.

4. Primary amines are obtained by reducing nitriles with sodium and alcohol (p. 109; cf. *Rakshit*, J. A. C. S. 1913, **35**, 444).



$$CH_3{\cdot}C{:}N + 4H = CH_3{\cdot}CH_2{\cdot}NH_2 \text{ (ethylamine).}$$

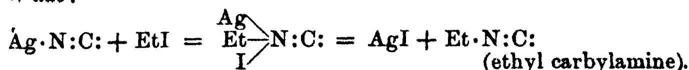
5. Metallic potassium or sodium frequently induces polymerization; thus methyl cyanide yields in this way **cyanmethine**, a mono-acid base crystallizing in prisms.

Aceto-nitrile, *Ethane-nitrile*, $CH_3{\cdot}CN$, b.-pt. 82° is present in the products of distillation from the vinasse of sugar beet and in coal-tar. **Propio-nitrile**, (*Propane-nitrile*), $C_2H_5{\cdot}CN$, **butyronitrile**, $C_3H_7{\cdot}CN$, and **valero-nitrile**, $C_4H_9{\cdot}CN$, are liquids of agreeable bitter-almond-oil odour; **palmito-nitrile**, $C_{15}H_{31}{\cdot}CN$, is like paraffin.

β. **Isocyanides, Isonitriles or Carbylamines.**—These are colourless liquids readily soluble in alcohol and ether, but only slightly soluble in water. They have a feeble alkaline reaction, an unbearable putrid odour, and poisonous properties, and boil somewhat lower than the isomeric nitriles.

Formation.—1. By heating an alkyl iodide with silver cyanide instead of potassium cyanide (*Gautier*), a double com-

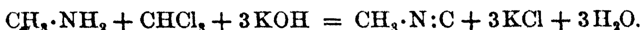
pound with silver cyanide being first formed, according to *Wade*:



$$Ag\cdot N:C: + EtI = \begin{matrix}Ag\\Et\\I\end{matrix}\!>\!N:C: = AgI + Et\cdot N:C:$$
(ethyl carbylamine).

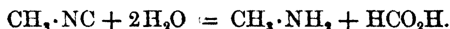
2. In small quantity, along with the nitrile, when a potassium alkyl-sulphate is distilled with potassium cyanide.

3. By the action of chloroform and alcoholic potash upon primary amines (*Hofmann*, 1869) (see pp. 66 and 111):



$$CH_3\cdot NH_2 + CHCl_3 + 3KOH = CH_3\cdot N:C + 3KCl + 3H_2O.$$

Behaviour.—1. The isonitriles differ fundamentally from the nitriles in their behaviour with water or dilute acids. When strongly heated with water, or with acids in the cold, they decompose into formic acid and a primary amine containing an atom of carbon less than themselves:



$$CH_3\cdot NC + 2H_2O = CH_3\cdot NH_2 + HCO_2H.$$

Unlike the nitriles, they are very stable towards alkalis.

2. The isonitriles are also capable of forming additive products with the halogens, HCl, H_2S, &c., compounds different from those given by the nitriles; thus, with HCl they yield crystalline salts which are rapidly decomposed by water into amine and formic acid.

3. Some of the isonitriles change into the isomeric nitriles when heated. According to *Wade* this change does not occur at all readily in the fatty series if the carbylamines are thoroughly dry. (J. C. S. 1902, **81**, 1596.)

Methyl isocyanide, $CH_3\cdot NC$, boils at 58°, and **ethyl isocyanide**, $C_2H_5\cdot NC$, at 82°.

Constitution of the Nitriles and Isonitriles.—The constitution of the nitriles follows from the readiness with which they can be hydrolysed to acids of the acetic series. In acetic acid we know that we have a methyl group directly attached to a carbon atom, *e.g.* $CH_3\cdot CO\cdot OH$, and since methyl cyanide on hydrolysis yields acetic acid, it also presumably contains the methyl group attached to carbon. The nitrogen atom, on the other hand, is eliminated, and is thus probably not directly bound to the alkyl radical. Consequently aceto-nitrile has the constitution $CH_3\cdot C{:}N$.

This constitutional formula is supported by a study of the product formed on reduction, namely $CH_3\cdot CH_2\cdot NH_2$.

In the case of the isonitriles, however, it is the nitrogen which must be directly bound to the alkyl radical, as their close connection with the amine bases shows, the amines being easily prepared from and reconverted into the isonitriles. The carbon atom of the cyanogen group, on the contrary, is eliminated as formic acid on decomposition with acid, and is consequently not directly united to the alkyl radical, but only through the nitrogen. The constitutional formula of methyl isocyanide is therefore either $CH_3 \cdot N \vdots C$ or $CH_3 \cdot N : C :$, with an unsaturated carbon atom (cf. Chap. L, E.2).

D. Amines or Nitrogen Bases of the Alkyl Radicals

By the introduction of alkyl radicals in place of hydrogen into the ammonia molecule, the important class of **ammonia bases** or **amines** is formed.

The amines containing small alkyl groups bear the closest resemblance to ammonia, and are even more strongly basic than the latter. They have an ammoniacal odour, give rise to white clouds with volatile acids, combine with hydrochloric acid, &c., to salts with evolution of heat, and yield platini- and auri-chlorides. Their aqueous solutions precipitate insoluble hydroxides from solutions of the salts of the heavy metals, and these precipitates are frequently soluble in excess.

The lowest members of this class are combustible gases readily soluble in water. The next are liquids of low boiling-point, also at first readily soluble; but the solubility in water, and also the volatility, decrease with an increase in molecular weight, until the highest members of the series, such as tricetylamine, $(C_{16}H_{33})_3N$, are at the ordinary temperature odourless solids of high boiling-point, insoluble in water but soluble in alcohol and ether, and readily combining with acids to form salts. All amines are considerably lighter than water.

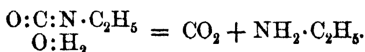
The quaternary ammonium hydroxides are solid and very hygroscopic, and exceedingly like potash in properties.

Classification.—The bases are divided into **primary, secondary, tertiary,** and **quaternary bases,** according as they contain 1, 2, 3, or 4 alkyl radicals; the three first are derived from ammonia, and the last from the hypothetical ammonium hydroxide, $NH_4 \cdot OH$. Characteristic of primary amines is the *amino* group, $\cdot NH_2$, of secondary, the *imino* group, $:NH$, and of tertiary, the N radical attached to three alkyl groups.

The system of *nomenclature* is simple, as indicated by the following examples:—$CH_3 \cdot NH_2$, **methylamine**; $C_3H_7 \cdot NH_2$, **propylamine**; $(C_2H_5)_2NH$, **di-ethylamine**; $(CH_3)_3N$, **trimethylamine**; and $N(C_2H_5)_4I$, **tetraethylammonium iodide**.

The alkyl radicals may be either saturated or unsaturated.

Modes of Formation.—1. Primary amines, *e.g.* methylamine, ethylamine, are obtained by heating alkyl cyanates with potash solution (*Wurtz*, 1848), just as cyanic acid itself yields ammonia and carbon dioxide:



$$\begin{matrix} O:C:N \cdot C_2H_5 \\ O:H_2 \end{matrix} = CO_2 + NH_2 \cdot C_2H_5.$$

2. By the direct introduction of the alkyl radical into ammonia by heating a concentrated solution of the latter with methyl iodide, chloride, or nitrate, ethyl iodide, &c. In this reaction an atom of hydrogen is first exchanged for an alkyl radical, and then the base produced combines with the halogen hydride, formed at the same time, to a salt, thus:—



$$\text{(I)} \qquad NH_2H + CH_3I = NH_2 \cdot CH_3, HI.$$

From the methylamine hydriodide thus produced, free methylamine can readily be obtained by distillation with potash:



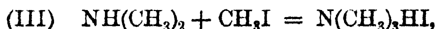
$$NH_2(CH_3), HI + KOH = NH_2(CH_3) + KI + H_2O.$$

The methylamine can now combine further with methyl iodide to hydriodide of dimethylamine:



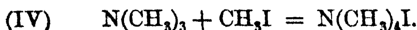
$$\text{(II)} \qquad NH_2(CH_3) + CH_3I = NH(CH_3)_2HI,$$

which, in its turn, yields the free base with potash. This latter can again combine with methyl iodide:



$$\text{(III)} \qquad NH(CH_3)_2 + CH_3I = N(CH_3)_3HI,$$

the salt so produced yielding trimethylamine as before. Finally, the trimethylamine can once more take up methyl iodide:



$$\text{(IV)} \qquad N(CH_3)_3 + CH_3I = N(CH_3)_4I.$$

The compound obtained, tetramethylammonium iodide, is, however, no longer a salt of an amine, but of an ammonium base, and is not decomposed on distillation with potash solution. The velocities of formation of quaternary ammonium iodides from tertiary amines and alkyl iodides have been determined by *Menschutkin*. The reaction has been shown

to be a bimolecular one. The velocity varies with the alkyl iodide employed, decreasing as the alkyl group becomes more complex. The solvent employed, for example, acetone, hexane, methyl alcohol, &c., also affects the velocity of formation to an enormous extent, *e.g.* the combination of ethyl iodide and try-ethylamine takes place some 250 times as readily in ethyl alcohol as in hexane solution.

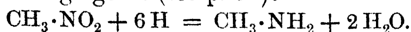
Primary and secondary bases can also be transformed into secondary and tertiary by warming with potassium alkyl-sulphates (B. 1891, **24**, 1678), or alkyl sulphates and alkali.

When several alkyl iodides are used in place of methyl iodide, **mixed amines**, *i.e.* amines containing different alkyl groups in the molecule, are obtained, *e.g.* **methyl-propylamine**, $NH(CH_3)(C_3H_7)$, **methyl-ethyl-propylamine**, $N(CH_3)(C_2H_5)(C_3H_7)$.

The reactions I to IV given above do not in reality follow each other in perfect order but go on simultaneously, the bases being partly liberated from the hydriodides by the ammonia, and so being free to react with more alkyl haloid. The product obtained by distillation with potash is therefore a mixture of all the three amines and ammonia.

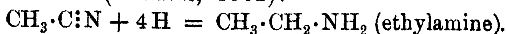
These cannot be separated by fractional distillation, and so their different behaviour with ethyl oxalate, OEt·CO·CO·OEt, is made use of for the purpose. Methylamine reacts with this ester to form chiefly (1) **dimethyl-oxamide**, $CH_3NH·CO·CO·NH·CH_3$ (solid), and (2) some **methyl-oxamic ester**, $OEt·CO·CO·NH·CH_3$ (liquid); dimethylamine yields (3) the **ethyl ester of dimethyl-oxamic acid**, $OEt·CO·CO·N(CH_3)_2$ (liquid), while trimethylamine does not react with the ethyl oxalate. Upon warming the product of the reaction on the water-bath, the latter base distils over, and the remaining compounds can then be separated by special methods (for which see B. **3**, 776; **8**, 760), and individually decomposed by potash, (1) and (2) yielding methylamine, and (3) dimethylamine. For separation by means of *Grignard* reagents, cf. *Hibbert* and *Wise*, J. C. S. 1912, **101**, 344.

3. The nitro-compounds yield primary amines when treated with acid reducing agents (see p. 98):



$$CH_3·NO_2 + 6\,H = CH_3·NH_2 + 2\,H_2O.$$

4. The nitriles, including hydrocyanic acid, are capable of taking up four atoms of hydrogen (see p. 105) and forming primary amines (*Mendius*, 1862):



$$CH_3·C{:}N + 4\,H = CH_3·CH_2·NH_2 \text{ (ethylamine)}.$$

5. Primary amines, in which $C < 6$, are prepared according to *Hofmann's* method, by the action of bromine and then of caustic-soda solution upon the amides of acids containing 1 carbon atom more than themselves (see Amides).

6. Primary amines likewise result from the reduction of the oximes or hydrazones (see pp. 133 and 141): for example, acetaldoxime:



$$CH_3\cdot CH{:}N\cdot OH + 4\,H = CH_3\cdot CH_2\cdot NH_2 + H_2O.$$

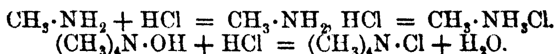
7. See Chap. XXVI, B., for preparation of amines from phthalimide.

Isomers.—Numerous isomers exist among the amines, thus:

	C_2H_7N.	C_3H_9N.	$C_4H_{11}N$.
Isomers	$NH_2(C_2H_5)$ $NH(CH_3)_2$	$NH_2(C_3H_7)$ $NH(CH_3)(C_2H_5)$ $N(CH_3)_3$	$NH_2(C_4H_9)$ $NH(CH_3)(C_3H_7)$ and $NH(C_2H_5)_2$ $N(CH_3)_2(C_2H_5)$

This kind of isomerism is the same as that of the ethers (p. 90), *i.e.* metamerism. From (C_3H_7) onwards, isomerism can also occur in the alkyl radicals. According to theory, as many amines C_n as alcohols C_{n+1} are capable of existence.

Behaviour.—1. The amines combine directly with acids (organic or inorganic) to form salts in exactly the same way as ammonia; the quaternary ammonium bases, however, react with acids, forming salts and eliminating water like potassium or ammonium hydroxide:



$$CH_3\cdot NH_2 + HCl = CH_3\cdot NH_2,\,HCl = CH_3\cdot NH_3Cl.$$
$$(CH_3)_4N\cdot OH + HCl = (CH_3)_4N\cdot Cl + H_2O.$$

The salts so obtained are white, crystalline compounds, readily soluble in water, and frequently hygroscopic. The chlorides form, with platinic chloride, sparingly soluble **platinichlorides** analogous to ammonium platinichloride, $(NH_4)_2PtCl_6$, *e.g.* methylamine platinichloride, $(CH_3NH_3)_2PtCl_6$.

The same applies to the **aurichlorides**, *e.g.* $C_2H_5NH_3AuCl_4$.

Strong alkalis, *e.g.* potassium hydroxide, decompose all the salts with the exception of the quaternary ammonium compounds yielding the free bases (and not ammonia).

2. Hydrolysing agents such as alkalis and acids do not affect the nitrogen bases of the alcohol radicals.

3. The different classes of amines are distinguished from

each other by the primary having 2 hydrogen atoms, the secondary 1, but the tertiary none replaceable by alkyl groups; the same applies to acyl groups, *e.g.* acetyl. The ultimate products obtained from isomeric amines by the action of methyl iodide are distinguished from one another by analysis. Thus of the three isomeric amines C_3H_9N, propylamine gives with methyl iodide, $C_3H_7 \cdot N(CH_3)_3I$, propyl-trimethylammonium iodide $= C_6H_{16}NI$; methyl-ethylamine gives $C_2H_5 \cdot N(CH_3)_3I$, ethyl-trimethylammonium iodide $= C_5H_{14}NI$; and trimethylamine gives $N(CH_3)_4I$, tetramethylammonium iodide $= C_4H_{12}NI$. An iodine estimation in the final product would immediately enable us to settle the constitution of the original amine.

The primary bases further differ from the others in their behaviour with chloroform, carbon disulphide, and nitrous acid.

4. Only the primary bases react with chloroform and alcoholic potash, with formation of isonitriles (p. 106).

5. When warmed with carbon disulphide in alcoholic solution, the primary and secondary, but not the tertiary, bases react to form derivatives of thiocarbamic acids. (See Carbonic Acid Derivatives.) Should the amines be primary ones, the characteristically smelling isothiocyanates are produced upon heating the thiocarbamic derivatives with a solution of $HgCl_2$ ("Senföl" reaction).

6. Nitrous acid reacts with the primary amines, forming alcohols, *e.g.*—



$$CH_3 \cdot NH_2 + H \cdot O \cdot NO = CH_3 \cdot OH + N_2 + H_2O.$$

A molecular rearrangement is occasionally met with, *e.g.* the production of isopropyl alcohol from *n*-propylamine.

Secondary bases yield with nitrous acid nitroso-compounds, *e.g.* "dimethyl-nitrosamine":



$$(CH_3)_2NH + NO \cdot OH = (CH_3)_2N \cdot NO + H_2O.$$

These nitrosamines are yellow-coloured volatile liquids of aromatic odour (*Geuther*). When reduced with acid-reducing agents, or when heated with alcohol and hydrochloric acid, they regenerate the secondary amines. Weak reducing agents, however, convert them into hydrazines (p. 115). The nitrosamines are frequently of great service in the purification of the secondary bases.

Nitrous acid forms salts with tertiary amines.

7. By the indirect action of nitric acid (B. 22, Ref. 295),

nitramines result, *i.e.* amines in which an amino-hydrogen atom has been replaced by the nitro-group, *e.g.* $CH_3 \cdot NH \cdot NO_2$, **methyl-nitramine.** Similarly, by the indirect introduction of an amino-group, hydrazines are formed, *e.g.* $CH_3 \cdot NH \cdot NH_2$, methyl-hydrazine.

8. While the amines are liberated from their salts by alkalis, the free bases of the quaternary ammonium salts, *e.g.* tetramethylammonium iodide, cannot be prepared from these by treatment with potash, because the products are soluble and non-gaseous, and hence an equilibrium is attained. The salts behave normally in aqueous solutions, for example, the iodides yield precipitates with silver nitrate, and are good electrolytes, The corresponding hydroxides, *e.g.* $N(CH_3)_4OH$, are obtained most readily by acting upon the iodides with moist silver oxide. These hydroxides are extraordinarily like caustic potash. They are colourless hygroscopic solids, readily soluble in water, and abstract carbon dioxide from the air. The solutions have strongly alkaline properties, are good electrolytes, and precipitate metallic hydroxides from solutions of their salts. When distilled they decompose, yielding the tertiary base, the tetramethyl base yielding in addition methyl alcohol, and the homologous bases olefine and water (*Braun*, A. 382, 1):



$$N(CH_3)_4 \cdot OH = N(CH_3)_3 + CH_3 \cdot OH.$$
$$N(C_2H_5)_4 \cdot OH = N(C_2H_5)_3 + C_2H_4 + H_2O.$$

They are of importance for the study of the valency of nitrogen. Their formation and general properties are most in harmony with the assumption of a penta- or quinque-valent nitrogen atom, *e.g.* $\begin{matrix} CH_3 \\ CH_3 \end{matrix} > N \begin{matrix} \diagup CH_3 \\ -CH_3 \\ \diagdown I \end{matrix}$, and not as a so-called molecular compound, $N(CH_3)_3$, CH_3I. (Cf. Trimethyl-sulphonium hydroxide.) The fact that the salts $N(CH_3)_2(C_2H_5) + C_2H_5Cl$ and $N(CH_3)(C_2H_5)_2 + CH_3Cl$ are identical, is in agreement with the former assumption. (*Meyer* and *Lecco.*) Lastly, optically active isomers are met with among the quaternary ammonium salts, a point which receives its readiest explanation from the dissymmetry of the molecule containing a quinquevalent nitrogen atom. (See Chap. XLVI, C.)

9. The quaternary iodides are resolved into tertiary base and alkyl iodide when heated. They combine with 2 or 4 atoms of bromine or iodine to tri- and penta-bromides or -iodides, *e.g.* $N(CH_3)_4 \cdot I \cdot I_4$ (dark needles), and $N(C_2H_5)_4I \cdot I_2$

(azure-blue needles). Such periodides readily lose the excess of iodine, and are hence relatively unstable. Hepta- and Ennea-iodides also exist.

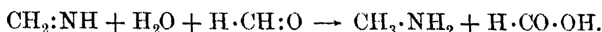
The following table gives the boiling-points of the various amines:—

	Primary.	Secondary.	Tertiary.
Methyl	− 6°	7°	3·5°
Ethyl	19°	56°	90°
n-Propyl.......	49°	110°	156°
n-Butyl........	76°	160°	215°
n-Octyl	176°	297°	366°

Methylamines. All three amines, particularly dimethylamine, are present in the brine in which herrings have been salted, and are derived from the decomposition of the fish. The secondary and tertiary amines are formed by the destructive distillation of the final residues from the molasses of beet-sugar factories. All three amines can be obtained from ammonia and formaldehyde (*Werner*, J. C. S. 1917, **111**, 844):



$$H{\cdot}CH{:}O + NH_3 \rightarrow H{\cdot}CH\langle^{OH}_{NH_2} \rightarrow H_2O + CH_2{:}NH,$$



$$CH_2{:}NH + H_2O + H{\cdot}CH{:}O \rightarrow CH_3{\cdot}NH_2 + H{\cdot}CO{\cdot}OH.$$

The formic acid can be further oxidized to CO_2 and H_2O, or can be converted into methyl formate. Formaldehyde is thus a methylating agent, just as a mixture of MeI or Me_2SO_4 and alkali. The methylamine can react with more formaldehyde, yielding dimethylamine, and the final stage is:



$$CH_2{:}O + 2\,NHMe_2 \rightarrow CH_2(NMe_2)_2 + H_2O,$$

and above 110°:



$$CH_2(NMe_2)_2 \rightarrow NMe_3 + CH_2{:}NMe,$$

no formic acid being produced.

When this method of formation of methylamines is used, the separation of the amines is based on the following facts: 1. Ammonium chloride is practically insoluble in a concentrated solution of methylamine hydrochloride. 2. Dimethyl-

amine hydrochloride is more soluble in water than the monomethylamine salt, and the former is soluble in chloroform solution and the latter not.

Methylamine, $CH_3 \cdot NH_2$, occurs in *Mercurialis perennis* and *annua* ("mercurialin"), in the distillate from bones and wood, and is formed when trimethylamine hydrochloride is heated at 285°.

It is most readily prepared from acetamide, caustic soda, and bromine. (B. **18**, 2737.) It is more strongly basic and even more soluble in water than ammonia, has a powerful ammoniacal and at the same time fishlike odour, and burns with a yellowish flame. Its aqueous solution, like that of ammonia, precipitates many metallic salts, frequently redissolving the precipitated hydroxides; unlike ammonia, it does not dissolve $Ni(OH)_2$ and $Co(OH)_2$.

The **hydrochloride**, $CH_3 \cdot NH_2$, HCl, forms large glistening plates, is very hygroscopic and readily soluble in alcohol; the **platinichloride** crystallizes in golden scales, and the sulphate forms an alum.

Dimethylamine, $(CH_3)_2NH$, occurs in Peruvian guano and pyroligneous acid, and is formed by decomposing nitroso-dimethyl-aniline by caustic-soda solution.

Trimethylamine, $(CH_3)_3N$, is widely distributed in nature, being found in considerable quantity in *Chenopodium vulvaria*, also in *Arnica montana*, in the blossom of *Cratægus oxyacantha*, and of pear. It has an ammoniacal and fishlike odour.

The tertiary amines can be oxidized by means of hydrogen peroxide to compounds of the type $(CH_3)_3N{:}O$, **trimethylamine oxide**, which are colourless crystalline bases.

Tetramethylammonium iodide, $N(CH_3)_4I$, is obtained in large quantity directly from $NH_3 + CH_3I$. It crystallizes in white needles or large prisms, and has a bitter taste.

Tetramethylammonium hydroxide, $N(CH_3)_4OH$, crystallizes in hygroscopic needles, and can be obtained by the action of alcoholic potash on an alcoholic solution of its chloride; potassium chloride is precipitated, and the hydroxide remains in solution. It forms salts, *e.g.* a platinichloride, sulphide, polysulphide, cyanide, &c.

Tetramethylammonium amalgam, $Hg(NMe_4)_x$, is formed during the electrolysis of the chloride in absolute alcohol at −34°, using a mercury cathode (J. A. C. S. 1911, **33**, 273).

Ethylamines. The ethylamines are usually manufactured from ethyl chloride and ammonia. They can be separated by

fractional distillation, using a ten-bulb column (J. C. S. 1916, **109**, 174). For the preparation of mono- and di-ethylamine from ethylbromide and ammonia, and the separation of their hydrochlorides by ammonia, see *Werner*, J. C. S. 1918, **113**, 899.

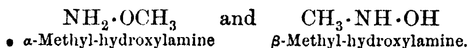
Ethylamine, $C_2H_5NH_2$, has a strongly ammoniacal smell and biting taste, mixes with water in every proportion, and burns with a yellow flame. It dissolves $Al(OH)_3$, but not $Fe(OH)_3$; also $Cu(OH)_2$ with difficulty, but not $Cd(OH)_2$. With bleaching powder it yields **ethyl-dichloro-amine,** $C_2H_5 \cdot NCl_2$, as a yellow oil of a most unpleasant piercing odour.

Tri-ethylamine, $(C_2H_5)_3N$, is an oily strongly alkaline liquid. The precipitates which it gives with solutions of metallic salts are mostly insoluble in excess of the precipitant.

When a substituted ammonium chloride is heated to a high temperature an alkyl chloride is formed, and when different alkyl groups are present in the molecule it is always the methyl group which is eliminated as chloride. Methyl chloride is prepared on a commercial scale by heating tetramethylammonium chloride obtained from beet-sugar residues.

E. Hydroxylamines; Hydrazines

The **Alkyl-hydroxylamines,** which are derived from hydroxylamine, $NH_2 \cdot OH$, just as the amines are from ammonia, belong to two different series, in accordance with the constitution of hydroxylamine, thus:—



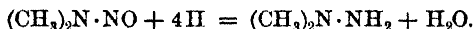
$NH_2 \cdot OCH_3$ and $CH_3 \cdot NH \cdot OH$

α-Methyl-hydroxylamine β-Methyl-hydroxylamine.

The compounds of the first series, which are obtained from the oxime ethers (p. 145), are—as ethereal compounds—tolerably stable, and do not reduce *Fehling's solution.* Those of the second series, which likewise result from certain oxime derivatives, but at the same time also from the reduction of the nitro-hydrocarbons (p. 99), very readily undergo change, reduce *Fehling's solution* even in the cold, and yield primary amines when further reduced (B. **23**, 3597; **24**, 3528; **25**, 1714).

E. Fischer (A. **190**, 67; **199**, 281; 294) has given the name of **hydrazines** to a series of peculiar bases, mostly liquid and

closely resembling the amines, but containing two atoms of nitrogen in the molecule, and differing from the latter especially by their capability of reducing *Fehling's solution*, for the most part even in the cold, and by the ease with which they are oxidized. They are derived from "Diamide" or "Hydrazine", $NH_2 \cdot NH_2$ (*Curtius* and *Jay*, J. pr. Ch. 1889, (2), **39**, 27). They are formed by the action of nascent hydrogen on the nitrosamines (p. 111):



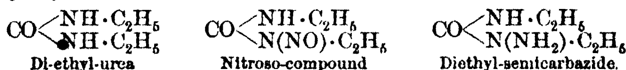
$$(CH_3)_2N \cdot NO + 4H = (CH_3)_2N \cdot NH_2 + H_2O.$$

Primary, secondary, tertiary, and quaternary hydrazines are known, according as 1, 2, 3, or 4 of the hydrogen atoms in $NH_2 \cdot NH_2$ are replaced by alkyl groups.

The secondary hydrazines exist in two isomeric forms, namely, $NHR \cdot NHR$ and $NH_2 \cdot NR_2$, which are known respectively as *symmetrical* and *unsymmetrical* secondary hydrazines.

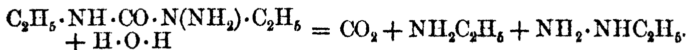
Methyl-hydrazine, $CH_3 \cdot NH \cdot NH_2$ (cf. A. 1889, **253**, 5). An excessively hygroscopic liquid, which fumes in the air, and has an odour similar to that of methylamine. B.-pt. 87°.

Ethyl-hydrazine, $C_2H_5 \cdot NH \cdot NH_2$. When di-ethyl urea is treated with nitrous acid a nitroso-compound is formed, which, on reduction with zinc dust and acetic acid, yields the so-called "diethyl-semicarbazide", and this decomposes, when heated with hydrochloric acid, into carbon dioxide, ethylamine, and ethyl-hydrazine:



$$CO{<}^{NH \cdot C_2H_5}_{NH \cdot C_2H_5} \qquad CO{<}^{NH \cdot C_2H_5}_{N(NO) \cdot C_2H_5} \qquad CO{<}^{NH \cdot C_2H_5}_{N(NH_2) \cdot C_2H_5}$$

Di-ethyl-urea — Nitroso-compound — Diethyl-semicarbazide.



$$\begin{matrix} C_2H_5 \cdot NH \cdot CO \cdot N(NH_2) \cdot C_2H_5 \\ + H \cdot O \cdot H \end{matrix} = CO_2 + NH_2C_2H_5 + NH_2 \cdot NHC_2H_5.$$

Ethyl-hydrazine is a colourless mobile liquid of ethereal and faintly ammoniacal odour, boiling at 100°. It is very hygroscopic, forms white clouds with moist air, dissolves in water and alcohol with evolution of heat, and corrodes cork and caoutchouc.

Diethyl-hydrazine, $(C_2H_5)_2N \cdot NH_2$, is prepared from diethylamine by transforming it into diethyl-nitrosamine by the nitrous-acid reaction, and then reducing the latter. It resembles ethyl-hydrazine closely:



$$(C_2H_5)_2N \cdot NO + 4H = (C_2H_5)_2N \cdot NH_2 + H_2O.$$

Tetra-ethyl-tetrazine, $(C_2H_5)_2 : N \cdot N : N \cdot N : (C_2H_5)_2$, a

colourless, strongly basic oil, volatile with steam, is formed when diethyl-hydrazine is heated with mercuric oxide.

The *constitution* of the hydrazines follows from their modes of formation. Since in diethyl-nitrosamine, $(C_2H_5)_2N \cdot NO$, for instance, the nitroso-group NO must be attached to the nitrogen of the amine and not to the carbon, judging from the ease with which it can be separated (p. 111), so the same linking of the atoms must be assumed in the hydrazines, which are formed from the nitroso-compounds by reduction, *i.e.* by exchange of O for 2H. The readiness with which diethyl-hydrazine is oxidized to diethylamine, *e.g.* by alkaline cupric oxide, is an agreement with such a formula. The hydrazines are relatively stable towards reducing agents.

For aliphatic Diazo and Triazo Compounds, see Chap. LI.

F. Alkyl Derivatives of Phosphorus, Arsenic, &c.

1. PHOSPHORUS

Just as amines are derived from ammonia, so from phosphuretted hydrogen, PH_3, are derived **primary**, **secondary**, and **tertiary phosphines** by the exchange of hydrogen for alkyl radicals, and to these must likewise be added quaternary compounds, the **phosphonium bases**. The phosphines correspond closely with the amines in composition and in some of their properties, *e.g.* they are not saponifiable. But they differ from them in the following points:—

1. Like phosphuretted hydrogen itself, the alkyl phosphines are only feebly basic; thus ethyl phosphine does not affect litmus, and its salts are decomposed by water. The salts of the secondary and tertiary compounds are not decomposed, thus showing that the presence of alkyl radicals tends to strengthen the basic properties of the compound.

2. Like phosphuretted hydrogen they are readily inflammable, and they are consequently rapidly oxidized in the air and readily take fire of themselves.

3. As the phosphorus atom in these compounds shows a tendency to pass from the ter- to the quinque-valent state, many of the phosphines behave as unsaturated compounds; they combine with oxygen, sulphur, halogens, &c., for example, $(CH_3)_3PO$, $(CH_3)_3PS$, $(CH_3)_3PCl_2$, and a compound $(CH_3)_3P, CS_2$, in the form of red plates. The products obtained on oxidation are characteristic, and may be regarded

as derived from phosphoric acid, $O:P(OH)_3$, by the replacement of one or more OH groups by one or more alkyl radicals.

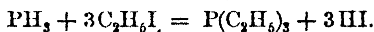
$CH_3\cdot PH_2$, with nitric acid, yields $CH_3\cdot PO\cdot(OH)_2$, **methyl phosphonic acid.**

$(CH_3)_2PH$, with nitric acid, yields $(CH_3)_2\cdot PO\cdot OH$, **dimethyl phosphinic acid.**

$(CH_3)_3P$, on oxidation in the air, yields $(CH_3)_3PO$, **trimethyl phosphine oxide.**

4. Corresponding with the disagreeable smell of phosphuretted hydrogen, they possess an excessively strong stupefying odour; thus ethyl phosphine has a perfectly overpowering smell, and excites on the tongue and deep down in the throat an intensely bitter taste.

Formation.—1. The tertiary phosphines and quaternary compounds are formed directly from phosphine and an alkyl iodide. (Cf. Amines, formation 2.)



$$PH_3 + 3C_2H_5I = P(C_2H_5)_3 + 3HI.$$

2. According to *Hofmann* (1871), primary and secondary phosphines are formed by heating phosphonium iodide and an alkyl iodide with zinc oxide, *e.g.*:



$$2C_2H_5I + 2PH_4I + ZnO = 2P(C_2H_5)H_2, HI + ZnI_2 + H_2O.$$

They can be separated from one another by decomposing the salts of the primary phosphines by water, as already mentioned.

3. The tertiary phosphines are produced from calcium phosphide and an alkyl iodide, a reaction first observed by *Thenard* in 1846;

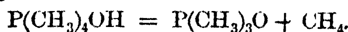
4. Also from phosphorus trichloride and zinc methyl, or magnesium alkyl iodides (*Auger* and *Billy*, C. 1904, **139**, 597).

5. The phosphonium salts are formed by the combination of tertiary phosphines with an alkyl haloid, and closely resemble the corresponding ammonium compounds.

Tri-ethyl phosphine, $P(C_2H_5)_3$, has no alkaline reaction. When concentrated it possesses a stupefying, and when dilute a pleasant hyacinth-like odour.

It forms a *peroxide*, PEt_3O_2, which is a powerful oxidizing agent, and hence tri-ethylphosphine can be used as an oxygen carrier, *e.g.* for the oxidation of indigotin by air.

Tetramethyl-phosphonium hydroxide, $P(CH_3)_4OH$, yields trimethyl-phosphine oxide and methane when heated:



$$P(CH_3)_4OH = P(CH_3)_3O + CH_4.$$

2. ARSENIC

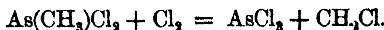
The similarity of arsenic to phosphorus and nitrogen is further exemplified by the analogous compounds which it forms with alkyl radicals. In virtue, however, of the more metallic character of arsenic, it does not show the same tendency to combine with alkyl radicals and hydrogen at the same time, but forms derivatives containing alkyl groups and electro-negative elements like chlorine or oxygen. Arsenic analogues of methylamine have been recently prepared, and are very unstable. (*Dehn*, Am. C. J. 1905, **33**, 120.) Trimethyl-arsine, analogous to trimethylamine and trimethylphosphine, is well known. As **primary** and **secondary compounds** we have methyl-arsine dichloride, $CH_3 \cdot AsCl_2$, dimethyl-arsine chloride, $(CH_3)_2AsCl$, and analogous substances. They are colourless liquids of stupefying odour, exerting in some cases an unbearable irritating action upon the mucous membrane. They do not possess basic properties. In addition to these there exist also quaternary compounds, **arsonium salts**, which are analogous to the quaternary phosphonium salts.

The halogen of the chlorine compounds is easily replaceable by its equivalent of oxygen. Thus, corresponding with the compound $R \cdot AsCl_2$ there is an oxide $R \cdot AsO$ and a sulphide $R \cdot AsS$, and with the chloride R_2AsCl an oxide $(R_2As)_2O$. These oxides, liquid or solid, are compounds of stupefying odour, and behave like basic oxides; hydrochloric acid reconverts them into the corresponding chlorides.

Here, also, the tendency of arsenic to change from the tervalent to the quinquevalent state is especially marked. The above chlorides and trimethyl-arsine itself all combine with two atoms of chlorine to compounds of the type AsX_5. The above oxygen compounds of the type AsX_3 and also trimethyl-arsine are consequently oxidizable to compounds containing one O atom or two OH groups more, acids or oxides which are also formed from the chlorides of the type AsX_5 by exchange of halogen for O or OH, *e.g.* cacodyl oxide, $(Me_2As)_2O$, to cacodylic acid, $Me_2As\lesssim^{OH}_{O}$. These products are therefore completely analogous to the phosphonic and phosphinic acids and phosphine oxides already described.

The compounds $As(CH_3)_xCl_{5-x}$, of the type AsX_5, when heated, decompose into methyl chloride and compounds $As(CH_3)_{x-1}Cl_{4-x}$, of the type AsX_3, this elimination of methyl

chloride taking place the more readily the fewer methyl groups are present in the molecule; thus $As(CH_3)_3Cl_2$ breaks up when somewhat strongly heated, $As(CH_3)_2Cl_3$ at 50°, and $As(CH_3)Cl_4$ at 0°, *i.e.* the last-named is only stable when in a freezing-mixture. When, therefore, chlorine acts upon $As(CH_3)Cl_2$ at the ordinary temperature, the reaction appears to be one of direct exchange of alkyl for chlorine, thus:—



$$As(CH_3)Cl_2 + Cl_2 = AsCl_3 + CH_3Cl.$$

It is interesting to note that, like free "methyl" ($CH_3\cdot$), the radical $\cdot As(CH_3)_2$ has no separate existence; cacodyl possesses the doubled formula $As_2(CH_3)_4$ ("Di-arsene-dimethyl")

The *tertiary arsines* are formed:

1. From sodium arsenide and alkyl iodide (*Cahours* and *Riche*):

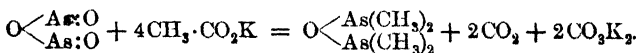


$$AsNa_3 + 3C_2H_5I = As(C_2H_5)_3 + 3NaI.$$

2. From arsenious chloride and (*a*) zinc alkyl (*Hofmann*) or (*b*) magnesium alkyl halide (*Pfeiffer*, B. 1904, **37**, 4620; *Sauvage*, C. 1904, **139**, 674; *Hibbert*, B. 1906, **39**, 160).

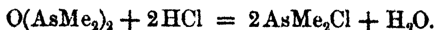
Trimethyl-arsine, $As(CH_3)_3$, and **triethyl-arsine**, $As(C_2H_5)_3$, are liquids sparingly soluble in water. They fume in the air, and are thereby oxidized to tri-methyl- or -ethyl-arsine oxide.

The **secondary arsines** are obtained from cacodyl and cacodyl oxide, which are formed when a mixture of potassium acetate and arsenious oxide is distilled (*Cadet*, 1760):



$$O\langle{}^{As:O}_{As:O} + 4CH_3\cdot CO_2K = O\langle{}^{As(CH_3)_2}_{As(CH_3)_2} + 2CO_2 + 2CO_3K_2.$$

The distillate of cacodyl and cacodyl oxide so obtained, and termed "alkarsin", fumes in the air and is spontaneously inflammable (*Cadet's* "fuming arsenical liquid"). Hydrochloric acid acts upon it to form cacodyl chloride (*Bunsen*, 1838), and caustic-potash solution gives pure **cacodyl oxide**, $As_2(CH_3)_4O$, a liquid of stupefying odour which produces nausea and unbearable irritation of the nasal mucous membrane; it boils without decomposition, and is insoluble in water and of neutral reaction. It yields salts with acids, *e.g.* **cacodyl chloride** with hydrochloric acid:



$$O(AsMe_2)_2 + 2HCl = 2AsMe_2Cl + H_2O.$$

The chloride is a liquid of even more stupefying odour and violent action than the oxide, and its vapour is spontaneously

inflammable. When heated with zinc clippings in an atmosphere of carbon dioxide, it yields the free **cacodyl**, $As_2(CH_3)_4$ (from κακώδης, "stinking"), a colourless liquid insoluble in water and boiling undecomposed at 170°, and of a horrible nauseous odour which produces vomiting. It is as readily inflammable in the air as the vapour of phosphorus, yielding the oxide when slowly brought in contact with it, and also combining directly with sulphur, chlorine, &c. Cacodyl plays, therefore, the part of a simple electro-positive element; it is a true "organic element" (*Bunsen*).

Cacodylic acid, $\frac{CH_3}{CH_3}>As\lessgtr^{O}_{OH}$, is crystalline, soluble in water, odourless, and poisonous. It forms crystallizable salts.

For more complex Arsenic Compounds, see Chap. LIII.

SUMMARY

		Compounds with Chlorine.	Oxides.	Acids.
Primary ..	Methyl-arsine dichloride, $AsMeCl_2$. B.-p. 133°.	Methyl-arsine tetra-chloride, $AsMeCl_4$.	Methyl-arsine oxide, AsMeO. B.-p. 95°.	Methyl-arsonic acid, $O:AsMe(OH)_2$. Solid plates.
Secondary	Cacodyl chloride, $AsMe_2Cl$. B.-p. 100°.	Cacodyl trichloride, $AsMe_2Cl_3$.	Cacodyl oxide, $(AsMe_2)_2O$. B.-p. 150°.	Cacodylic acid, $O:AsMe_2 \cdot OH$. Prisms. M.-p. 200°.
Tertiary...	Trimethyl-arsine, $AsMe_3$. B.-p. 70°.	Trimethyl-arsine dichloride, $AsMe_3Cl_2$.	Trimethyl-arsine oxide, $AsMe_3O$. Solid.	

3. ANTIMONY, BORON, AND SILICON COMPOUNDS

Alkyl derivatives of antimony are also known, *e.g.* **Trimethylstibine**, a spontaneously inflammable liquid with a garlic odour; **Antimony pentamethyl**, $SbMe_5$, a non-poisonous volatile liquid; and **Tetramethylstibonium hydroxide**, $SbMe_4 \cdot OH$, a solid resembling caustic potash. Mixed derivatives, *e.g.* $SbEt_2Ph$ and $SbEtPh_2$ can be obtained by

heating a mixture of $SbCl_3$ and $SbPh_3$, first forming $SbPhCl_2$ and $SbPh_2Cl$, and then treating these with magnesium ethyl bromide. The trialkyl derivatives of bismuth, *e.g.* $BiMe_3$, are unstable, and bismuthonium compounds are not known.

Boron tri-ethyl, $B(C_2H_5)_3$ (*Frankland*), is a spontaneously inflammable liquid which burns with a green flame with deposition of much soot; and **boron trimethyl,** $B(CH_3)_3$, an analogous gas of an unbearable stinking smell.

The silicon compounds (*Friedel* and *Crafts*), in contradistinction to the foregoing, resemble methane and the paraffins rather than the spontaneously inflammable silicon hydride, and are very stable in the air. **Tetramethyl silicane,** $Si(CH_3)_4$, is a mobile liquid similar to pentane, and floats on water. **Tetraethyl silicane** or **Siliconpremonane,** $SiEt_4$, is also known, and gives rise to numerous derivatives corresponding with those of tetraethyl methane, *e.g.* $SiC_8H_{19}Cl$, $SiC_8H_{19}\cdot O\cdot CO\cdot CH_3$, $SiC_8H_{19}\cdot OH$, **Siliconony alcohol,** &c. Cf. Chap. XLVI, B., and for nomenclature, *Kipping*, J. C. S. ,1912, 423. Numerous organic derivatives of silicon have been described by *Kipping* during the years 1901–1929.

G. Organo-Metallic Compounds; Grignard Reagents.

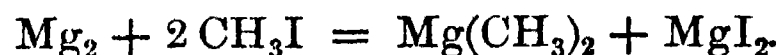
Most of the important metals form definite compounds with alkyl groups. The composition of these organo-metallic or metallo-organic compounds almost always corresponds with that of the metallic chlorides from which they are derived by the replacement of halogen by alkyl. They are colourless, mobile liquids which boil, without decomposition, at relatively low temperatures; they often decompose violently with water and burn explosively in the air, but in other cases they are stable, both in water and air. To the former category belong the magnesium, zinc, and aluminium alkyls, and to the latter the mercury, lead, and tin compounds. As most of the compounds are volatile, their molecular weights can be determined, and hence the valencies of the respective metals determined, as the alkyl radicals are monovalent. Examples are: $ZnMe_2$, $CdMe_2$, $HgEt_2$, $AlMe_3$, $PbMe_4$, $SnEt_4$, &c.

Compounds are also known which contain halogen as well as alkyl radicals combined with a metal. They behave like salts. The halogen in them can be replaced by hydroxyl, whereby basic compounds result, compounds which are often much more strongly basic than the corresponding metallic hydroxides, in accordance with the electro-positive character

of the alcohol radical. Such hydroxides or oxides cannot be volatilized without decomposition. Compounds of this type, *e.g.* $CH_3 \cdot Mg \cdot I$, are very readily prepared from their components ($Mg + CH_3I$) in dry ethereal solution, and are largely made use of as synthetical reagents.

The organo-metallic compound may be prepared—

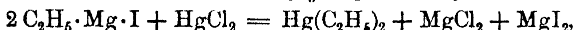
1. By treating the alkyl halide with the metal in question. In this way zinc-, magnesium-, and mercury-alkyls are got:



$$Mg_2 + 2\,CH_3I = Mg(CH_3)_2 + MgI_2.$$

The mixed organo-metallic compounds (p. 125), *e.g.* $CH_3 \cdot Mg \cdot I$ or $C_2H_5 \cdot Zn \cdot I$, are probably formed as intermediate products.

2. Numerous metallic compounds have been prepared by double decomposition between zinc-alkyl and the metallic chloride, or more recently by the action of the mixed magnesium compounds on the metallic chloride. *Pfeiffer* (B. 1904, 319, 1125, 4617), *Hibbert* (B. 1907, 160) have prepared numerous tin, lead, and mercury compounds by this method:

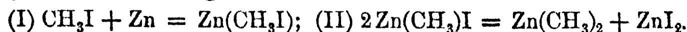


$$2\,C_2H_5 \cdot Mg \cdot I + HgCl_2 = Hg(C_2H_5)_2 + MgCl_2 + MgI_2,$$

and a compound $Pb(C_6H_5)_3$ analogous to triphenylmethyl (Chap. L), has also been isolated (B. 1919, 2165). *Kipping* has used Grignard reagents for synthesing various organo-silicon compounds (J. C. S., 1907–1915).

Potassium- and Sodium methyl, $K(CH_3)$ and $Na(CH_3)$, **Potassium- and Sodium ethyl**, $K(C_2H_5)$ and $Na(C_2H_5)$, and similar derivatives, *e.g.* sodium benzyl, $Na \cdot CH_2 \cdot C_6H_5$, are formed by the action of the alkali metal on the corresponding mercury compound in dry benzene. They are mostly colourless amorphous solids and burn in contact with the air. The benzyl compound is a red crystalline compound and its ethereal solution is an electrolyte (*Schlenck* and *Holz*, B. 1917, **50**, 262). They combine with carbon dioxide, yielding the alkali salts of carboxylic acids.

Zinc methyl or methide, $Zn(CH_3)_2$ (*Frankland*, 1849), is prepared according to method 1:



$$(I)\ CH_3I + Zn = Zn(CH_3I);\quad (II)\ 2\,Zn(CH_3)I = Zn(CH_3)_2 + ZnI_2.$$

The first stage is completed upon warming, and the second upon distilling the resulting product. The zinc is conveniently used in the form of the "copper-zinc couple", and the reaction is facilitated by the addition of ethyl acetate, the reason for this not being known. Zinc methyl is a colourless, mobile, strongly refracting liquid of very piercing and repulsive smell.

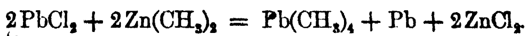
B.-pt. 46°; sp. gr. 1·39. It is spontaneously combustible, and burns with a brilliant reddish-blue flame (the zinc flame), with formation of zinc oxide, but may be distilled in an atmosphere of carbon dioxide. When the supply of oxygen is limited, zinc methoxide, $Zn(OCH_3)_2$, is formed. It reacts violently with water, yielding methane and $Zn(OH)_2$, and with methyl iodide gives ethane. It is employed in the preparation of secondary and tertiary alcohols and of ketones. Iodine converts it into **zinc-methyl iodide**, $ZnCH_3I$, white plates (see above), and methyl iodide; an excess of iodine yields zinc iodide and methyl iodide.

Zinc ethyl, $Zn(C_2H_5)_2$, b.-pt. 118°, sp. gr. 1·18, closely resembles zinc methide.

The mercury compounds, $HgMe_2$ and $HgEt_2$, are produced by method of formation 1, also by method 2. They are colourless liquids of peculiar sweetish and unpleasant odour, and boil respectively at 95° and 159°. They are permanent in the air, but inflammable, and both—especially the methyl compound—are very poisonous.

Aluminium methyl, $Al(CH_3)_3$, is spontaneously inflammable and decomposes violently with water. B.-pt. 130°. For vap. dens. see B. **22**, 551.

Lead tetramethyl, $Pb(CH_3)_4$, and **ethyl**, $Pb(C_2H_5)_4$ (*Cahours*). These are formed according to method 2, curiously with separation of lead:



$$2PbCl_2 + 2Zn(CH_3)_2 = Pb(CH_3)_4 + Pb + 2ZnCl_2.$$

They are stable in the air, and are interesting from the lead in them being tetravalent. The **hydroxide**, $Pb(CH_3)_3 \cdot OH$, forms pointed prisms, smells like mustard, and is a strong alkali; thus, it saponifies fats, drives out ammonia from its salts, precipitates metallic salts, &c. The compound $Pb_2(C_2H_5)_6$ is also known.

The tin compounds are similar (*Ladenburg, Frankland*).

Tin tetramethyl, $Sn(CH_3)_4$, **Tin tetraethyl**, $Sn(C_2H_5)_4$, **Tin triethyl**, $Sn_2(C_2H_5)_6$, **Tin dimethyl**, $Sn_2(CH_3)_4$, &c., are of interest as indicating the tetravalence of tin.

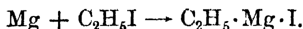
GRIGNARD REAGENTS

For a number of years the zinc alkyl compounds were of considerable importance, as they were used for synthesizing different types of carbon compounds, more particularly hydro-

carbons, secondary and tertiary alcohols and ketones, and the structural formulæ given to products were largely based on these syntheses.

Since 1900 the metallic alkyls have been almost completely replaced by the mixed organo-metallic compounds introduced by *Grignard* (C. R. 1900, **130**, 1322; 1901, **132**, 336, 558), and hence commonly known as *Grignard* reagents. Within recent years no single group of compounds has proved of such value in synthetic chemistry as these reagents.

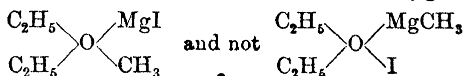
The reagents are prepared by dissolving dry magnesium ribbon or filings in a dry ethereal solution of an alkyl bromide or iodide:



$$Mg + C_2H_5I \rightarrow C_2H_5 \cdot Mg \cdot I.$$

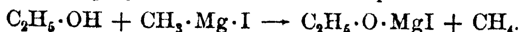
Aromatic compounds in which halogen is attached either to the side chain or nucleus react in a similar manner (cf. Chap. XIX, B.).

The *Grignard* reagent does not exist as such in the ethereal solution, but in the form of an additive compound with ether, *e.g.* $MgCH_3I, (C_2H_5)_2O$. This additive compound can be isolated by removing the ether and warming the residue under reduced pressure at 100°, and is relatively stable, and undoubtedly may be regarded as a derivative of quadravalent oxygen, probably



(*Grignard*, Bull. Soc., 1907, [IV], **1**, 255, cf. however **Meisenheimer** and **Caspari** [B. 1921, 1655] who regard them as complex compounds). The alkyl magnesium halides are also formed when benzene is used, but a much higher temperature is required, and a trace of ether or of a tertiary amine accelerates the reaction.

The *Grignard* reagents react readily with water or with alcohols yielding hydrocarbons and a compound $R \cdot O \cdot MgI$:



$$C_2H_5 \cdot OH + CH_3 \cdot Mg \cdot I \rightarrow C_2H_5 \cdot O \cdot MgI + CH_4.$$

Based on this reaction, a process has been worked out for estimating hydroxy groups in carbon compounds (*Hibbert* and *Sudborough*, J. C. S. 1904, **85**, 933; *Zerewitinoff*, B. 1907, **40**, 2023), and consists in measuring the volume of methane evolved. In a somewhat similar manner the reaction may be used for differentiating primary, secondary, and tertiary amines, as the first contains two, the second one, and the last no reactive hydrogen atoms in their molecules (*Sudborough* and

Hibbert). With H_2O_2 a *Grignard* reagent yields the corresponding alcohol, *e.g.* isobutyl or isoamyl alcohol.

As synthetic reagents the *Grignard* compounds may react in one of three ways:

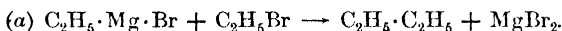
1. With reactive hydrogen atoms, *e.g.* in ·OH, ·COOH, $\cdot NH_2$, ·NHR, ⋮CH, or the hydrogen atom of a reactive methylene group. The product formed from an alcohol and a *Grignard* reagent can, by the action of an alkyl halide, yield an ether:



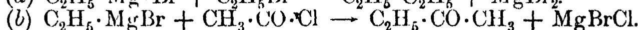
$$R\cdot CH_2\cdot OH \rightarrow R\cdot CH_2\cdot OMgI;$$
$$R\cdot CH_2\cdot OMgI + C_2H_5Br \rightarrow R\cdot CH_2\cdot OC_2H_5.$$

If a primary or secondary amine is used and the product treated with methyl sulphate, the N-methyl derivative of the amine is formed.

2. With the halogen atom of an alkyl halide or an acid chloride.



(*a*) $C_2H_5\cdot Mg\cdot Br + C_2H_5Br \rightarrow C_2H_5\cdot C_2H_5 + MgBr_2.$



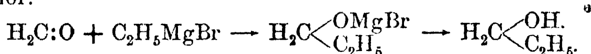
(*b*) $C_2H_5\cdot MgBr + CH_3\cdot CO\cdot Cl \rightarrow C_2H_5\cdot CO\cdot CH_3 + MgBrCl.$

As a rule the reaction (*b*) does not stop at the formation of the ketone, but proceeds further as described under 3.

3. The addition of CH_3 and MgI to unsaturated linkings; the commonest of these is the addition to the ·C:O, carbonyl, group, but can also occur at C:C, C:N, &c.

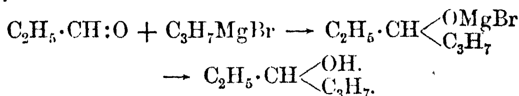
The syntheses of alcohols—primary, secondary, and tertiary—is based on the addition of the *Grignard* to a carbonyl group and the reaction of the product with water or a dilute acid.

(*a*) With formaldehyde H·CH:O, the product is a primary alcohol:



$$H_2C{:}O + C_2H_5MgBr \rightarrow H_2C\begin{matrix}\diagup OMgBr\\ \diagdown C_2H_5\end{matrix} \rightarrow H_2C\begin{matrix}\diagup OH\\ \diagdown C_2H_5\end{matrix}.$$

(*b*) With other aldehydes the product is a secondary alcohol:



$$C_2H_5\cdot CH{:}O + C_3H_7MgBr \rightarrow C_2H_5\cdot CH\begin{matrix}\diagup OMgBr\\ \diagdown C_3H_7\end{matrix}$$
$$\rightarrow C_2H_5\cdot CH\begin{matrix}\diagup OH\\ \diagdown C_3H_7\end{matrix}.$$

(*c*) With a ketone the product is a tertiary alcohol:



$$(CH_3)_2C{:}O + (CH_3)_2C\begin{matrix}\diagup OMgBr\\ \diagdown C_2H_5\end{matrix} \rightarrow (CH_3)_2C\begin{matrix}\diagup OH\\ \diagdown C_2H_5\end{matrix}.$$

with the exception of certain *aa*-substituted ketones when secondary alcohols are formed (Annales, 1921, IX, **16**, 354).

Tertiary alcohols are also formed from acid chlorides or esters and a *Grignard* reagent (cf. p. 75). In these reactions it is probable that ketones are first formed by the exchange of the Cl of the acid chloride or the OEt of the ester for the alkyl group of the *Grignard* reagent.

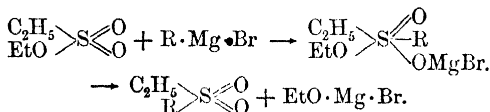
It is clear that if dialdehydes, diketones, or esters of dibasic acids are used dihydric alcohols (glycols) will be formed.

In the preparation of an alcohol, especially in the aromatic series, it frequently happens that an olefine hydrocarbon is formed instead of the alcohol, especially when a high temperature is used, and is to be attributed to the elimination of Br·Mg·OH from the additive compound of the ketone or aldehyde and *Grignard* reagent (cf. Chap. XVIII, B.)

Grignard reagents are extremely useful for preparing the alkyl and aryl derivatives of many metals and non-metals, (cf. p. 123), by the reaction between the halogen derivatives of these and *Grignard* compounds.

ββ-Dialkyl hydroxylamines $N(C_2H_5)_2$·OH are formed by the action of alkyl magnesium bromides on nitro paraffins, on esters of nitrous acid, and even esters of nitric acid (J. C. S., 1921, 251).

Grignard compounds react with the ethyl esters of aliphatic sulphonic acids yielding sulphones (p. 93.)



The esters of aromatic sulphonic acid do not react in the same manner (*Ferns* and *Lapworth*, J. C. S., 1912, 283).

With dibromo derivatives of saturated hydrocarbons magnesium can behave in one of two ways. (*a*) It can remove the halogen as magnesium bromide yielding an olefine or even a cyclic hydrocarbon, *e.g.* 1:2-dibromoethane yields ethylene and 1:3-dibromopropane yields cyclopropane with some propylene (*Grignard.*) (*b*) With compounds such as 1:4-dibromobutane, 1:5-dibromopentane and 1:7-dibromoheptane, a certain amount of the dimagnesium compound $BrMg(C_nH_{2n})_xMgBr$ is formed, but there is no formation of cyclic or unsaturated hydrocarbons and no mono magnesium compound of the type $BrMg(C_nH_{2n})_xBr$ can be isolated (*Von Braun* and *Sobecki*, B. 1911, 1918). A tribromo compound of the type CH_2Br·CHBr·$(CH_2)_n$·CH_2Br reacts with magnesium giving an un-

saturated *Grignard* reagent, viz., $CH_2:CH(CH_2)_n \cdot CH_2 \cdot MgBr$ (B. 1919, 1713).

The magnesium compounds of the type $BrMg \cdot (CH_2)_n \cdot MgBr$ have been used for preparing cyclic compounds containing mercury and other elements as part of the ring (Chap. XXXIII). For use in preparation of benzene hydrocarbons see Chap. XVIII, A; acids, p. 149 and Chap. XXVI, formation 5*h*; ketones, p. 140; aldehydes, Chap. XXV, B.; tertiary alcohols, Chap. XXX; sulphinic acids, Chap. XXIII; synthetic terpenes, Chap. XLI, B. II; complex silicon compounds, Chap. XLVI, B. For a summary of recent work on *Grignard* reagents cf. Hepworth (J. Ind., 1922, **41**, T. 7).

A reaction analogous to the *Grignard* reaction and of considerable importance for synthetical purposes is the *Reformatsky* reaction (cf. p. 272), in which zinc, an alkyl iodide (or more frequently the ester of a brominated acid), and a ketone are used. It may be regarded as analogous to the use of a *Grignard* reagent.

The unsaturated compound $CH_2:AlI$ from methylene iodide and Al in the presence of ether forms an additive compound with iodine (C. R., 1922, **174**, 112).

V. ALDEHYDES AND KETONES, $C_nH_{2n}O$

The aldehydes and ketones are substances which are respectively formed by the oxidation of the primary and secondary alcohols, the oxidation consisting in the elimination of two atoms of hydrogen from each molecule of alcohol.

The aldehydes are formed from the primary alcohols, and are easily converted by further oxidation into the corresponding acids containing an equal number of carbon atoms, oxygen being taken up. They possess in consequence strongly reducing properties.

The ketones result from the oxidation of the secondary alcohols, and are more difficult to oxidize further; they do not possess reducing properties. Their oxidation does not lead to acids containing an equal number of carbon atoms in the molecule, but to others containing a smaller number, the carbon chain being broken.

The lower members of both classes are neutral liquids of peculiar smell, readily soluble in water and readily volatile, only CH_2O being gaseous. As the number of carbon atoms

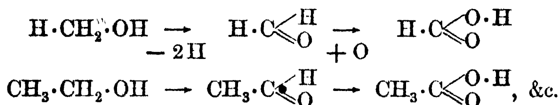
increases they become less soluble, and their odour becomes less marked with rise of boiling-point until the highest members are solid, odourless like paraffin, and only capable of being distilled under reduced pressure.

The aldehydes closely resemble the ketones as regards modes of formation and also in many of their properties.

Both groups of compounds contain the carbonyl :C:O group, but in the aldehydes this is always attached to a hydrogen atom, and also to an alkyl group or a second hydrogen, *e.g.* $CH_3 \cdot CO \cdot H$ and $H \cdot CO \cdot H$, whereas in a ketone it is attached to two alkyl groups, *e.g.* $C_2H_5 \cdot CO \cdot C_2H_5$.

A. Aldehydes

The homologous series of the aldehydes, $C_nH_{2n}O$, corresponds exactly with that of the acids, $C_nH_{2n}O_2$. They form a group of compounds exactly intermediate between the primary alcohols and the fatty acids. Each primary alcohol by the loss of hydrogen yields an aldehyde, and this by the addition of oxygen yields a fatty acid:



Their boiling-points are decidedly lower than those of the corresponding alcohols, and rise, in the normal aldehydes, at first by about 27° for each CH_2, and later on by a less amount.

Nomenclature.—The name aldehyde is derived from *al*(cohol), *dehyd*(rogenatus), *i.e.* an alcohol from which hydrogen has been removed. The various aldehydes are named according to the acids to which they give rise on oxidation. For example, $H \cdot CHO$ formaldehyde, $CH_3 \cdot CHO$, acetaldehyde, &c. According to the Geneva Congress, the aldehydes receive names ending in *al*, *e.g.* ethanal for acetaldehyde.

Modes of Formation.—1. By the regulated oxidation of the primary alcohols, $C_nH_{2n+1}OH$, by potassium dichromate or manganese dioxide and dilute sulphuric acid; often slowly by atmospheric oxygen, especially in the presence of bone-black or platinum:



$$CH_3 \cdot CH_2 \cdot OH + O = CH_3 \cdot CH{:}O + H_2O.$$

2. From the acids of the acetic series, by distilling a mixture of their calcium or barium salts with calcium or barium formate (*Limpricht*). The formic acid acts in this instance as a reducing agent, producing calcium carbonate, thus:—



$$CH_3\cdot COOca + HCOOca = CH_3\cdot CHO + CaCO_3. \quad (ca = \tfrac{1}{2}Ca.)$$

3. From the dihalogen substitution products of the hydrocarbons containing the group $\cdot CHX_2$, by superheating with water or by boiling with water and PbO:



$$CH_3\cdot CHCl_2 + H_2O = CH_3\cdot CHO + 2HCl.$$

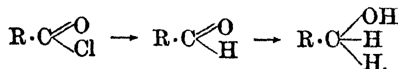
4. From *Grignard* reagents (p. 124), and ethyl formate or ethyl orthoformate. Also by heating alcohols with metals or metallic oxides (Chap. XLIX, A., Oxidation).

Constitution.—In the oxidation of the primary alcohols, $R\cdot CH_2\cdot OH$, to their corresponding acids, $R\cdot CO\cdot OH$, the alkyl radical R remains unaltered. It must consequently also remain unchanged in the intermediate products of the oxidation, viz. the aldehydes, which therefore possess the constitution $R\cdot CHO$:



$CH_3\cdot CH_2\cdot OH$	$CH_3\cdot CHO$	$CH_3\cdot CO\cdot OH$
Alcohol	Aldehyde	Acetic acid.

The aldehydes thus contain the group $\cdot CHO$, either $\cdot C\cdot OH$ or $\cdot C\langle^{O}_{H}$. The former is improbable, as the aldehydes do not, as a rule, give reactions characteristic of compounds containing hydroxyl radicals. All their properties point to the presence of the :C:O group. The characteristic grouping of all aldehydes is thus the $\cdot C\langle^{H}_{O}$ group. This is confirmed by the fact that an acid chloride $R\cdot C\langle^{O}_{Cl}$ on reduction yields a primary alcohol and in certain cases an aldehyde can be isolated (Chap. VII, B.):



$$R\cdot C\langle^{O}_{Cl} \rightarrow R\cdot C\langle^{O}_{H} \rightarrow R\cdot C\begin{cases}OH\\H\\H.\end{cases}$$

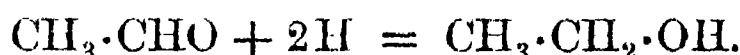
Isomers.—Isomerism in the aldehydes is caused solely by isomerism in the alkyl radicals R, which are combined with the group $\cdot CHO$, and therefore contain an atom of carbon less. Otherwise the aldehydes—from C_3H_6O on—are isomeric with the ketones, with the oxides of the olefines (*e.g.* aldehyde with

ethylene oxide, C_2H_4O), and with the alcohols of the allylic series.

Behaviour. — The aldehydes are distinguished by being exceptionally chemically active.

1. The aldehydes are very readily oxidizable, slowly even by the air alone, and quickly by chromic acid, salts of the noble metals, &c. They consequently reduce an ammoniacal solution of silver and often one of copper; this reaction is characteristic and is especially delicate in the presence of caustic-soda solution. (Formation of silver mirror.)

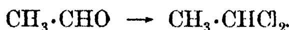
2. The aldehydes are easily reduced by nascent hydrogen, *e.g.* sodium amalgam and dilute acid or zinc dust and glacial acetic acid, to the primary alcohols from which they are derived by oxidation, *e.g.*:



$$CH_3 \cdot CHO + 2H = CH_3 \cdot CH_2 \cdot OH.$$

A glycol is formed as a by-product, *e.g.* butylene glycol, $C_4H_8(OH)_2$, from C_2H_4O.

3. Phosphorus pentachloride and trichloride convert the aldehydes into ethylidene chloride and analogous dichloro-substitution products of the hydrocarbons:



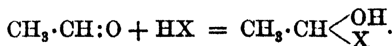
$$CH_3 \cdot CHO \rightarrow CH_3 \cdot CHCl_2.$$

4. Additive reactions. According to *Perkin* (J. C. S. 1887, 808), a solution of acetaldehyde in water contains a certain amount of the hydrate, $CH_3 \cdot CH(OH)_2$. (Cf. Chloral hydrate.) This compound is extremely unstable, and has never been isolated in a pure form. In those reactions in which it might be formed, its anhydride (acetaldehyde) is invariably produced, *e.g.* $CH_3 \cdot CHCl_2$ with alkali yields $CH_3 \cdot CH:O$ as final product, and not $CH_3 \cdot CH(OH)_2$, although this is probably formed as an intermediate substance.

Thus we conclude *that two hydroxyl groups attached to the same carbon atom cannot as a rule exist together*, but a molecule of water is eliminated, and an aldehyde or ketone is formed. In particular cases only can compounds with two such hydroxyl groups exist (see Chloral).

If, in place of water, $NaHSO_3$, NH_3, HCN, &c., be employed, direct addition to the aldehydes is readily observed, and in all these reactions it is concluded that the addition occurs at the expense of the doubly-united oxygen atom. A hydrogen atom of the substance in question attaches itself to the oxygen of the aldehyde, with formation of a hydroxyl group, while

the residual X (*e.g.* CN), which was originally bound to the afore-mentioned H atom, becomes united to the carbon:

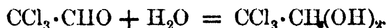


$$CH_3\cdot CH{:}O + HX = CH_3\cdot CH{<}^{OH}_{X}.$$

Cf. additive reactions of the olefines (p. 46).

The most important additive reactions are:—

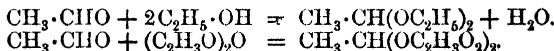
(*a*) Combination with water, which would lead to a dihydric alcohol, does not as a rule take place, for the reasons already given. Should the alkyl radical of the aldehyde, however, contain several negative atoms, *e.g.* Cl, then the hydrates are capable of existence, for instance chloral hydrate:



$$CCl_3\cdot CHO + H_2O = CCl_3\cdot CH(OH)_2.$$

But even in these cases the tendency for water to separate is too great to allow of such hydrates behaving as dihydric alcohols; they react rather, for the most part, exactly like the aldehydes themselves. (Cf. Pyroracemic and Mesoxalic acids.)

(*b*) Occasionally, compounds with alcohol or acetic acid, *e.g.* R·CH(OEt)(OH), or R·CH(OH)(OAc), are met with. They are, however, extremely unstable. When the aldehyde is heated with alcohol or acetic anhydride, stable ethers or esters of the hypothetical glycols are obtained:



$$CH_3\cdot CHO + 2C_2H_5\cdot OH = CH_3\cdot CH(OC_2H_5)_2 + H_2O.$$
$$CH_3\cdot CHO + (C_2H_3O)_2O = CH_3\cdot CH(OC_2H_3O_2)_2.$$

The compounds obtained from alcohols, the so-called **"acetals"** (see p. 136), are also formed by the partial oxidation of primary alcohols, and are hydrolysed by sulphuric acid.

(*c*) The aldehydes combine with sodium hydrogen sulphite, $NaHSO_3$, &c., to crystalline compounds, readily soluble in water but sparingly in alcohol, *e.g.* C_2H_4O, $NaHSO_3$, $\frac{1}{2}H_2O$. These are to be regarded as sulphite derivatives of the ethylidene glycols, for instance, $CH_3\cdot CH(OH)(\cdot O\cdot SO_2Na)$. (B. 1928, 179). They are almost invariably decomposed when heated with alkalis or acids and regenerate the aldehydes, and are of importance for the separation of aldehydes from mixtures.

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bisulphite compounds, they are advantageously used for the purification of aldehydes, as they readily yield the aldehydes when warmed with dilute acid. (See p. 135.)

(*e*) The aldehydes combine with hydrocyanic acid to form nitriles of higher acids; thus acetic aldehyde yields the compound $CH_3 \cdot CH<^{OH}_{CN}$, **ethylidene cyanhydrin.** This reaction is largely made use of in the preparation of certain hydroxy acids, as the cyanhydrins, when hydrolized, yield hydroxy acids, *e.g.* $CH_3 \cdot CH<^{OH}_{COOH}$, lactic acid.

The action is accelerated by the presence of an alkali or of a metallic cyanide, *i.e.* of the CN ion (cf. *W. J. Jones*, J. C. S. 1914, **105**, 1560).

(*f*) An interesting additive reaction is that between an aldehyde and a *Grignard* compound (p. 126). Thus acetaldehyde and magnesium ethyl iodide yield $^{CH_3}_{C_2H_5}>CH \cdot OMgI$, and this with water gives methyl-ethyl-carbinol, $^{CH_3}_{C_2H_5}>CH \cdot OH$.

5. The aldehydes show great tendency to polymerize. (See pp. 12 and 47.) In the case of formaldehyde this polymerization occurs spontaneously at the ordinary temperature. Acetaldehyde is polymerized upon the addition of small quantities of hydrochloric, sulphuric, or sulphurous acid, zinc chloride, carbonyl chloride, &c., to para-aldehyde, $C_6H_{12}O_3$, $= (C_2H_4O)_3$, at the ordinary temperature, and to meta-aldehyde, $(C_2H_4O)_3$, at 0°.

Another type of polymerization is the aldol condensation (see pp. 134 and 138).

6. Aldehyde and several of its homologues, when heated with caustic-soda solution, are transformed into a reddish-brown resin termed **aldehyde-resin**, a product insoluble in water but soluble in alcohol, and possessing a peculiar odour. Other aldehydes are transformed by alkalis into a mixture of equivalent amounts of alcohol and acid, thus:—

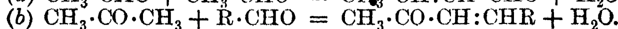


$$2\,RCOH + H_2O = RCH_2OH + R \cdot CO_2H.$$

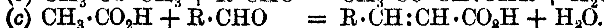
7. The aldehydes show a great tendency to form *condensation* products with aldehydes, ketones, acids, &c. (See Croton-aldehyde, Cinnamic acid, &c.)



(*a*) $CH_3 \cdot CHO + CH_3 \cdot CHO = CH_3 \cdot CH{:}CH \cdot CHO + H_2O.$

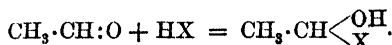


(*b*) $CH_3 \cdot CO \cdot CH_3 + R \cdot CHO = CH_3 \cdot CO \cdot CH{:}CHR + H_2O.$



(*c*) $CH_3 \cdot CO_2H + R \cdot CHO = R \cdot CH{:}CH \cdot CO_2H + H_2O.$

the residual X (*e.g.* CN), which was originally bound to the afore-mentioned H atom, becomes united to the carbon:

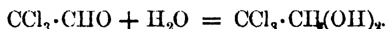


$$CH_3\cdot CH{:}O + HX = CH_3\cdot CH\begin{matrix}\diagup OH\\ \diagdown X\end{matrix}.$$

Cf. additive reactions of the olefines (p. 46).

The most important additive reactions are:—

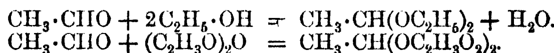
(*a*) Combination with water, which would lead to a dihydric alcohol, does not as a rule take place, for the reasons already given. Should the alkyl radical of the aldehyde, however, contain several negative atoms, *e.g.* Cl, then the hydrates are capable of existence, for instance chloral hydrate:



$$CCl_3\cdot CHO + H_2O = CCl_3\cdot CH(OH)_2.$$

But even in these cases the tendency for water to separate is too great to allow of such hydrates behaving as dihydric alcohols; they react rather, for the most part, exactly like the aldehydes themselves. (Cf. Pyroracemic and Mesoxalic acids.)

(*b*) Occasionally, compounds with alcohol or acetic acid, *e.g.* $R\cdot CH(OEt)(OH)$, or $R\cdot CH(OH)(OAc)$, are met with. They are, however, extremely unstable. When the aldehyde is heated with alcohol or acetic anhydride, stable ethers or esters of the hypothetical glycols are obtained:



$$CH_3\cdot CHO + 2C_2H_5\cdot OH = CH_3\cdot CH(OC_2H_5)_2 + H_2O.$$
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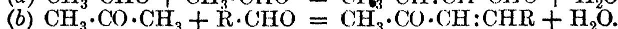


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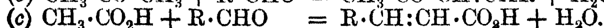
7. The aldehydes show a great tendency to form *condensation* products with aldehydes, ketones, acids, &c. (See Croton-aldehyde, Cinnamic acid, &c.)



(*a*) $CH_3 \cdot CHO + CH_3 \cdot CHO = CH_3 \cdot CH{:}CH \cdot CHO + H_2O.$



(*b*) $CH_3 \cdot CO \cdot CH_3 + R \cdot CHO = CH_3 \cdot CO \cdot CH{:}CHR + H_2O.$



(*c*) $CH_3 \cdot CO_2H + R \cdot CHO = R \cdot CH{:}CH \cdot CO_2H + H_2O.$

It is probable that in all these condensations direct addition first occurs; for example, in (*a*) aldol, $CH_3 \cdot CH(OH) \cdot CH_2 \cdot CHO$, is first formed, and then by the loss of water forms croton aldehyde, $CH_3 \cdot CH:CH \cdot CHO$. (See p. 138.)

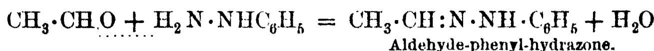
8. With hydroxylamine the aldehydes yield the so-called **Aldoximes**, water being eliminated (*V. Meyer*, B. **15**, 2778).



$$CH_3 \cdot CH:O + H_2N \cdot OH = CH_3 \cdot CH:N \cdot OH + H_2O.$$

For the conditions under which oximes are formed, see B. **23**, 2760.

9. The aldehydes react with hydrazines to form the so-called **Hydrazones**, water being eliminated. Phenylhydrazine is the reagent usually employed:



$$CH_3 \cdot CH.O + H_2N \cdot NHC_6H_5 = CH_3 \cdot CH:N \cdot NH \cdot C_6H_5 + H_2O$$

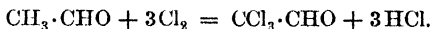
Aldehyde-phenyl-hydrazone.

Most of the phenylhydrazones are somewhat sparingly soluble in alcohol, crystallize very readily, and are made use of in identifying different aldehydes. On reduction they yield primary amines:



$$CH_3 \cdot CH:N \cdot NH \cdot C_6H_5 + 4H = CH_3 \cdot CH_2 \cdot NH_2 + NH_2 \cdot C_6H_5.$$

10. Moist chlorine and bromine act upon the aldehydes as substituents; thus, from acetaldehyde chloral is obtained:



$$CH_3 \cdot CHO + 3Cl_2 = CCl_3 \cdot CHO + 3HCl.$$

11. Sulphuretted hydrogen converts the aldehydes into thioaldehydes. These are compounds of unpleasant aromatic odour, which show the same peculiarities of polymerization as the aldehydes (*Klinger*). (Cf. *E. Baumann*, B. **23**, 60; **24**, 1419, 3591.)

Reactions 8 and 9 may also be regarded as condensations. It is possible that in all these reactions direct addition first occurs, and that water is subsequently eliminated.

Tests for aldehydes:

(1) Behaviour with ammoniacal silver-nitrate solution (p. 131, and also B. **15**, 1629).

(2) Behaviour with alkaline bisulphites (p. 132).

(3) Behaviour with phenyl-hydrazine and hydroxylamine (see above).

(4) Aldehydes colour a solution of fuchsine which has been

decolorized by sulphurous acid (*Schiff's* reagent) an intense violet-red; some ketones and chloral, but not chloral hydrate, produce the same effect. (B. **13**, 2343; Bull. Soc. Chim. 1894, **11**, 692.)

Formaldehyde, *Methanal*, H·CH:O, may be regarded as the oxide of the divalent methylene radical, CH_2:. An aquesus solution containing methyl alcohol is obtained by passing the vapour of the latter mixed with air over heated copper or platinized asbestos. **Formalin** is the commercial 40 per cent solution obtained by using copper. It is also a product of the action of ozone or of oxygen on methane (B. 1912, **45**, 3915; J. Ind., 1922, **41**, 303T). It can be condensed to a volatile liquid boiling at −21°. It is largely used as an antiseptic and disinfectant, also for condensing with phenols to yield the product known as Bakelite, and recently has come into use as a methylating agent.

Its chief polymeric forms are:

(1) **Para-formaldehyde**, probably $(CH_2O)_2$, a white mass soluble in water; (2) **trioxy-methylene**, probably $(CH_2O)_3$, a crystalline compound which passes into formaldehyde again when volatilized; (3) **formose** (Chap. XIV, A.), a mixture of several compounds of the nature of glucose. On account of this facility for undergoing polymerization, formaldehyde in all probability plays an important part in assimilation by plants.

It does not form an additive compound with ammonia, but condenses to the complex compound $C_6H_{12}N_4$, hexamethyleneamine.

By its combination with hydrochloric acid, **chloro-methyl alcohol** (*chloro-methanol*), $CH_2Cl(OH)$, and **hydroxy-chloro-methyl ether** (*chloromethane-oxy-methanol*), $CH_2Cl·O·CH_2OH$, are formed. Both of these are colourless liquids, which react in many respects like formaldehyde itself.

Methylal, $CH_2(OCH_3)_2$ (see Acetals, p. 132), is frequently made use of instead of formaldehyde, for carrying out condensation reactions. It is employed in medicine as a soporific, and is also used as an extractive for certain scents. B.-pt. 42°.

Acetaldehyde, *Ethanal*, *Aldehyde*, $CH_3·CHO$, was formerly termed "acetyl hydride", $C_2H_3O·H$ (*Fourcroy* and *Vauquelin*, 1800; composition established by *Liebig* in 1835). It is prepared by passing ammonia gas into an ethereal solution of the crude aldehyde, obtained by oxidizing alcohol with $K_2Cr_2O_7$ + H_2SO_4 and drying over $CaCl_2$, washing the precipitated aldehyde-ammonia with ether, and finally distilling it with dilute sulphuric acid. It is obtained in large quantity as a by-

product in the first portions of the distillate "**First Runnings**" in the manufacture of spirit. For its production in place of vinyl alcohol, $CH_2{:}CH\cdot OH$, from acetylene, see pp. 53 and 84.

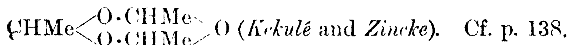
It is produced commercially by the addition of water to acetylene under the influence of mercury and its salts (p. 53 and Chap. L, H). also from alcohol vapour by passing over heated copper.

It is a colourless mobile liquid, boils at 21°, and has sp. gr. about 0·8. Its odour is aromatic and suffocating, and produces a kind of cramp in the chest when inhaled. It burns with a luminous flame, dissolves sulphur, phosphorus, and iodine, and is readily soluble in water, alcohol, and ether.

Para-aldehyde, $C_6H_{12}O_3$, is a liquid sparingly soluble in water. It melts at 10°, and boils at 124°, *i.e.* more than 100° above that of aldehyde, and is used as a soporific.

Meta-aldehyde, $(C_2H_4O_3)_3$, crystallizes in white prisms insoluble in water, and sublimes at a little over 100°, but is partially reconverted into aldehyde. (B. **14**, 2271; **40**, 4341.)

Meta-aldehyde is changed back again into ordinary aldehyde by prolonged heating to 115° in sealed tubes, and also, as is the case with para-aldehyde, by distillation with somewhat dilute sulphuric acid. Para-aldehyde reacts in the same way as ordinary aldehyde with PCl_5, but not with NH_3, $NaHSO_3$, $AgNO_3$, and NH_2OH. This constitution of para-aldehyde may be represented as:



With regard to these and other polymeric compounds, the general rule has been proved to hold that, in the case of bodies of similar constitution, the one of simpler composition is the more soluble, possesses the lower melting-point, and is the more easily vaporized.

Acetal, $CH_3\cdot CH(OC_2H_5)_2$, boils at 104°. It is usually obtained by the partial oxidation of ethyl alcohol with manganese dioxide and sulphuric acid, the acetaldehyde first formed condensing with the alcohol with the production of acetal. This, as well as methylal, is frequently used instead of aldehyde for the carrying out of condensation reactions (see p. 133).

Propaldehyde, $C_2H_5\cdot CHO$, is present in wood-tar. Normal **heptaldehyde** (*œnanthal*), $C_7H_{14}O$, is obtained by the dry distillation of castor-oil under diminished pressure, &c.

Chloral, *2-trichloro-ethanal*, $CCl_3 \cdot CHO$, is a liquid which boils at 98°, and which—when impure—easily changes into a solid polymeric modification, meta-chloral, but is regenerated from this upon heating. It combines readily with water to **chloral hydrate**, $CCl_3 \cdot CH(OH)_2$ (see p. 132, *a*), and with alcohol to **chloral alcoholate**, $CCl_3 \cdot CH(OH)(OC_2H_5)$, and **trichloro-acetal**, $CCl_3 \cdot CH(O \cdot C_2H_5)_2$. The end product of the action of chlorine upon alcohol consists chiefly of the last three substances. They are all colourless crystalline compounds, which are converted into chloral by distilling with sulphuric acid, and rectifying over lime.

Chloral is an oily liquid with a sharp, characteristic odour. It combines with sodium bisulphite, ammonia, hydrocyanic acid, and acetic anhydride, and reduces an ammoniacal solution of silver oxide. It is readily oxidized to trichloracetic acid, and decomposed by alkali into chloroform and an alkali formate (cf. p. 66).

For properties of aldehydes and their derivatives, cf. *Harries*, C. Z. 1916, **ii**, 991.

Chloral hydrate, $CCl_3 \cdot CH(OH)_2$, forms large colourless crystals readily soluble in water, melting at 57°, and boiling with dissociation at 97°. It acts as a soporific and antiseptic. Sulphuric acid converts it into chloral.

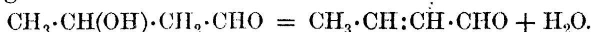
UNSATURATED ALDEHYDES

Acrolein, *Acr-aldehyde, propenal*, $CH_2{:}CH \cdot CHO$, is formed by the oxidation of allyl alcohol, by the distillation of fats, and by heating glycerol with anhydrous magnesium sulphate (B. 1912, **45**, 204). It is a liquid boiling at 52°, of pungent odour (the smell of burning fat being due to it), and of violent action upon the mucous membrane of the eyes. It unites in itself the properties of an aldehyde and of an unsaturated carbon compound, and therefore combines with ammonia and with bromine; it also unites with hydrogen bromide to *bromopropyl aldehyde*, $CH_2Br \cdot CH_2 \cdot CHO$.

When distilled, acrolein-ammonia yields picoline, C_6H_7N (see Pyridine bases); and crotonaldehyde-ammonia, by an analogous reaction, collidine, $C_8H_{11}N$.

Acrolein can combine with two atoms of bromine to acrolein dibromide (dibromoprop-aldehyde), $CH_2Br \cdot CHBr \cdot CHO$, a compound which is of importance in the synthesis of the sugars. (See Synthesis of Monoses.)

Croton-aldehyde, $CH_3 \cdot CH:CH \cdot CHO$. When acetaldehyde is left for some time in contact with dilute hydrochloric acid or sodium hydroxide, polymerization occurs, and a substance termed **aldol**, or α-hydroxy-butyraldehyde, is obtained, $CH_3 \cdot CH(OH) \cdot CH_2 \cdot CHO$. The constitution of aldol follows from its properties. It cannot be readily converted back into acetaldehyde, and in this respect differs from the other polymeric forms, viz. meta- and para-aldehyde. This difference is due to the fact that in the aldol condensation the union of the molecules has been brought about between carbon atoms, and hence the relative stability. Aldol when distilled or in presence of dehydrating agents yields croton-aldehyde, water being eliminated.



$$CH_3 \cdot CH(OH) \cdot CH_2 \cdot CHO = CH_3 \cdot CH:CH \cdot CHO + H_2O.$$

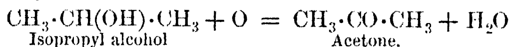
On oxidation it yields crotonic acid.

B. Ketones

The lowest member of the series, Acetone, contains three atoms of carbon. The higher members, from C_{12} on, are solid. They are all lighter than water; *e.g.* the sp. gr. of acetone is 0·81 at 0°.

Occurrence.—Acetone is present in urine, methyl-nonyl ketone in oil of rue, and also with homologues in cocoanut oil.

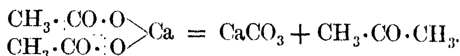
Modes of Formation.—1. By the oxidation of secondary alcohols; just as in the conversion of a primary alcohol to an aldehyde, this oxidation consists in the withdrawal of two hydrogen atoms from each molecule of the alcohol:



$$\underset{\text{Isopropyl alcohol}}{CH_3 \cdot CH(OH) \cdot CH_3} + O = \underset{\text{Acetone.}}{CH_3 \cdot CO \cdot CH_3} + H_2O$$

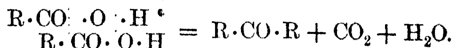
Many primary and secondary alcohols are decomposed into hydrogen and aldehyde (or ketone) when heated in contact with a catalyst (see Chap. XLIX).

2. By the dry distillation of the calcium or barium salts of fatty acids at about 400°:



$$\begin{matrix} CH_3 \cdot CO \cdot O \\ CH_3 \cdot CO \cdot O \end{matrix} > Ca = CaCO_3 + CH_3 \cdot CO \cdot CH_3.$$

Some of the ketones of high molecular weight may be obtained by heating fatty acids with phosphorus pentoxide (*Kipping*), or even heating the acids at 295° for three hours:

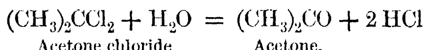


$$\begin{matrix} R \cdot CO \cdot O \cdot H \\ R \cdot CO \cdot O \cdot H \end{matrix} = R \cdot CO \cdot R + CO_2 + H_2O.$$

When a mixture of two calcium salts is taken a **mixed ketone** is formed; thus calcium acetate and calcium propionate yield methyl ethyl ketone in addition to dimethyl and diethyl ketones. As a rule, in addition to the mixed ketone, the two simple ketones, *e.g.* $(CH_3)_2CO$ and $(C_2H_5)_2CO$, are also formed.

A modification of this method is to pass the vapour of the acid over heated carbonate of calcium, barium, or manganese (cf. Chap. XLIX, E.).

3. From dichlorides containing the group $C\cdot CCl_2\cdot C$:



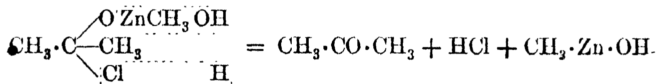
$$(CH_3)_2CCl_2 + H_2O = (CH_3)_2CO + 2\,HCl$$

Acetone chloride — Acetone.

It is probable that the chlorine atoms are first replaced by hydroxyls, yielding the glycol, $CMe_2(OH)_2$, which immediately eliminates H_2O, yielding the ketone, CMe_2O.

4. By the action of zinc alkyl upon an acid chloride, *e.g.* acetyl chloride, $CH_3\cdot COCl$.

An additive compound is first formed, $CH_3\cdot C\begin{cases}OZnCH_3\\CH_3\\Cl\end{cases}$, which must be quickly decomposed by water, otherwise tertiary alcohols are produced:

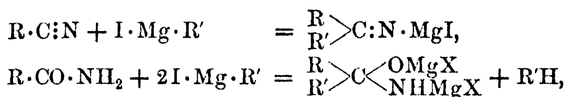


$$CH_3\cdot C\begin{cases}O\,ZnCH_3\;OH\\CH_3\\Cl\qquad\;\;H\end{cases} = CH_3\cdot CO\cdot CH_3 + HCl + CH_3\cdot Zn\cdot OH.$$

This method of formation, which was devised by *Freund* in 1861, allows of the preparation of any possible ketone by using the requisite zinc alkyl and acid chloride.

At the same time it elucidates, together with method 2, the *constitution* of the ketones from the constitution of the corresponding acids. Conclusions regarding constitution based on the latter method must be accepted with a considerable amount of reserve unless supported by other arguments, since in reactions which occur at high temperatures intramolecular rearrangements can readily occur. Theoretically, therefore, ketones are compounds which contain the carbonyl group, CO, linked on both sides with an alkyl radical, $R\cdot CO\cdot R$. If the alcohol radicals are the same, "simple" ketones result; and if different, "**mixed**" ketones. A compound with less than 3 C atoms is thus impossible.

Ketones have been synthesised by the action of organo-magnesium compounds on nitriles or acid amides, *e.g.*:



$$R\cdot C{:}N + I\cdot Mg\cdot R' = {R \atop R'}{>}C{:}N\cdot MgI,$$

$$R\cdot CO\cdot NH_2 + 2I\cdot Mg\cdot R' = {R \atop R'}{>}C{<}{OMgX \atop NHMgX} + R'H,$$

and these with water yield $R\cdot CO\cdot R'$. (*Blaise*, C. 1901, **132**, 38, **133**, 299.)

5. From the ketonic acids or their esters, *e.g.* acetoacetic ester, $CH_3\cdot CO\cdot CH_2\cdot CO\cdot OC_2H_5$, by warming with moderately dilute sulphuric acid or with dilute alkalis. This important reaction will be treated of at greater length under acetoacetic ester.

6. By the addition of water to homologues of acetylene, $CH_3\cdot C{:}CH + H_2O = CH_3\cdot CO\cdot CH_3$. This reaction occurs at relatively high temperatures, or may be brought about indirectly by the aid of sulphuric acid, or solutions of mercuric salts

Isomers.—The ketones exhibit the same isomerism as the secondary alcohols. This isomerism depends on the one hand upon the isomerism within the alkyl groups, *e.g.* dipropyl ketone and di-*iso*-propyl ketone, which are linked together by the CO group, and on the other by the position of the oxygen atom in the carbon chain (position isomerism); thus, $C_4H_9\cdot CO\cdot CH_3$ is isomeric with $C_3H_7\cdot CO\cdot C_2H_5$.

The aldehydes containing an equal number of carbon atoms in the molecule are always isomeric with the ketones, since both classes of compounds are formed from isomeric alcohols by the withdrawal of 2 H.

Further, acetone is isomeric with allyl alcohol. Such an isomerism of a saturated with an unsaturated compound is termed "saturation isomerism" (cf. p. 90).

Nomenclature.—The usual name is formed by adding the suffix ketone to the name of the alkyl groups present; *e.g.* $(C_2H_5)_2CO$, diethyl ketone; $CH_3\cdot CO\cdot C_2H_5$, methylethyl ketone, &c. The names of the simple ketones are also derived from the acids which yield them, *e.g.* "Valerone" $(C_4H_9)_2CO$, from valeric acid.

The systematic names of the ketones are formed by taking the name for the corresponding hydrocarbon, adding the suffix one to indicate the O replacing 2 H, and then a number to indicate the position of the O atom, *e.g.* $CH_3\cdot CO\cdot CH_2\cdot CH_3$, butan-2-one, &c.

Behaviour.—1. Reagents which give rise to nascent hydrogen reduce the ketones to secondary alcohols: $(CH_3)_2CO + 2H = (CH_3)_2CH \cdot OH$. Small amounts of pinacones (p. 200) are formed at the same time.

Drastic reducing agents, such as amalgamated zinc and concentrated hydrochloric acid, reduce both aldehydes and ketones to the saturated hydrocarbons (*Clemmensen*, B. 1913, **46**, 1837).

2. Oxidizing agents, *e.g.* $K_2Cr_2O_7$, and dilute H_2SO_4, slowly convert the ketones into acids or ketones containing a smaller number of carbon atoms in the molecule (not—as in the case of the aldehydes—into acids containing an equal number), the carbon chain being broken.



$$CH_3 \cdot CO \cdot CH_3 + 4O = CH_3 \cdot COOH + CO_2 + H_2O.$$

Oxidation analogous to that of the aldehydes is clearly impossible. Oxidation to a ketonic acid is theoretically possible with certain ketones, *e.g.* $R \cdot CO \cdot CH_3 \rightarrow R \cdot CO \cdot CO_2H$, but occurs only rarely. The usual oxidation leads to a scission of the molecule in such a manner that in a mixed ketone the CO group remains attached to the smaller alkyl group. Thus $CH_3 \cdot CO \cdot C_3H_7$ on oxidation yields mainly acetic $CH_3 \cdot CO_2H$ and propionic $C_2H_5 \cdot CO_2H$ acids; but at the same time a small amount is oxidized to a mixture of carbonic and butyric acids (B. **25**, R. 121).

The ketones do not possess reducing properties.

3. Phosphorus pentachloride, PCl_5, converts the ketones into the corresponding dichlorides, acetone, for instance, into acetone chloride, $(CH_3)_2CCl_2$.

4. Additive reactions. (*a*) The ketones do not as a rule combine with water and alcohol, for the reasons given under the aldehydes.

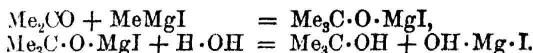
(*b*) With ammonia they yield complex condensation products, *e.g.* di-acetone-amine, $C_6H_{13}NO$, tri-acetone-amine, $C_9H_{17}NO$ (*Heintz*); this reaction is more complicated than that with the aldehydes, 2 or 3 molecules of acetone combining with 1 molecule of ammonia, with elimination of water.

(*c*) The ketones which contain the group $CH_3 \cdot CO \cdot$, and a few other relatively simple ketones, combine with sodium hydrogen sulphite to crystalline compounds, *e.g.* acetone to $(CH_3)_2C \lt^{OH}_{O \cdot SO_2Na}$, H_2O, which can be converted back into the ketone by distillation with sodium-carbonate solution. This

very important reaction is made use of in separating and puri fying the ketones. *Stewart* has recently (J. C. S. 1905, **87**, 185) studied the comparative rates at which some of these compounds are formed.

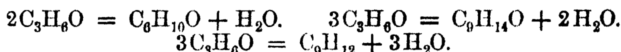
(*d*) With hydrocyanic acid they yield hydroxy-nitriles, as in the case of the aldehydes; *e.g.* $(CH_3)_2C<^{OH}_{CN}$.

(*e*) Ketones readily form additive compounds with *Grignard's* reagents, and when decomposed with water these yield tertiary alcohols (see p. 75):



$$Me_2CO + MeMgI = Me_3C{\cdot}O{\cdot}MgI,$$
$$Me_3C{\cdot}O{\cdot}MgI + H{\cdot}OH = Me_3C{\cdot}OH + OH{\cdot}Mg{\cdot}I.$$

5. The ketones, unlike the aldehydes, do not possess the property of polymerizing, but they form condensation products. Just as aldehyde is converted into croton-aldehyde, so is acetone, by the action of many reagents—*e.g.* CaO, KOH, HCl, and H_2SO_4—converted, with elimination of water, into **mesityl oxide**, $C_6H_{10}O$, **phorone**, $C_9H_{14}O$, or **mesitylene**, C_9H_{12}, according to the conditions (see these substances):



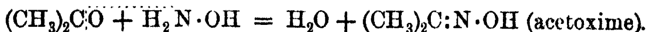
$$2C_3H_6O = C_6H_{10}O + H_2O. \quad 3C_3H_6O = C_9H_{14}O + 2H_2O.$$
$$3C_3H_6O = C_9H_{12} + 3H_2O.$$

Analogous condensations also ensue with other ketones or aldehydes under the influence of dilute caustic soda or of sodium ethoxide (B. **20**, 655). In this way the more complicated ketones are formed (A. **218**, 121).

6. Sulphuretted hydrogen converts the ketones into thio-compounds, *e.g.* acetone into thio-acetone, $CH_3{\cdot}CS{\cdot}CH_3$ (B **16**, 1368), or their polymers.

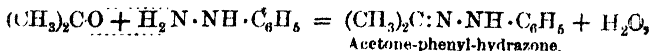
7. Halogens give rise to substitution products.

8. Like the aldehydes, the ketones—even C_{35}—react with hydroxylamine, yielding oximes, which are termed **Ketoximes** (*V. Meyer*, B. **15**, 1324, 2778; **16**, 823, 1784, &c.):



$$(CH_3)_2C{:}O + H_2N{\cdot}OH = H_2O + (CH_3)_2C{:}N{\cdot}OH \text{ (acetoxime).}$$

9. They react in an analogous manner with phenyl-hydrazine, $C_6H_5{\cdot}NH{\cdot}NH_2$ (*E. Fischer*, B. **17**, 572), with the formation of **phenyl-hydrazones** (p. 134):



$$(CH_3)_2CO + H_2N{\cdot}NH{\cdot}C_6H_5 = (CH_3)_2C{:}N{\cdot}NH{\cdot}C_6H_5 + H_2O,$$

Acetone-phenyl-hydrazone.

and with semicarbazide, $NH_2 \cdot CO \cdot NH \cdot NH_2$, or its hydrochloride yielding **semicarbazones**, *e.g.* $(CH_3)_2C:N \cdot NH \cdot CO \cdot NH_2$, which crystallize well and have definite melting-points. **Acetaldehyde-semicarbazone** melts at 162°, and **acetone-semicarbazone** at 189°. The three reagents, hydroxylamine, phenyl-hydrazine, and semicarbazide, are extremely useful in detecting and identifying aldehydes and ketones.

10. Nitrous acid (ethyl nitrite and sodium ethylate) gives rise to **iso-nitroso-ketones**, *e.g.* iso-nitroso-acetone, $CH_3 \cdot CO \cdot CH:N \cdot OH$, by replacement of H_2 by the group $:N \cdot OH$ (oximino). When hydrolyzed, the $:N \cdot OH$ group is replaced by oxygen, and diketones or aldehydo-ketones are formed.

Acetone, *2-Propanone,* $CH_3 \cdot CO \cdot CH_3$. The formula was established by *Liebig* and *Dumas* in 1832. It is present in very small quantity in normal urine, in the blood, in serum, &c., but in much larger quantity in pathological cases such as acetonuria and diabetes mellitus. It is a product of decomposition of cellulose, and is found in wood spirit. It is usually manufactured from calcium acetate made from pyroligneous acid (p. 156), or by the fermentation of starch, *e.g.* maize by a particular species of bacterium, which yields *n*-butyl alcohol and acetone (J. Ind. 1919, **38,** 273 T.: cf. Chap. XLVIII, A.).

It is a liquid of peculiar pungent odour; boils at 57·5°, and has sp. gr. 0·81 at 0°. It is soluble in water, but may be salted out from its aqueous solution, and it is also miscible with alcohol and ether. $KMnO_4$ does not oxidize it in the cold, but CrO_3 converts it into acetic and carbonic acids.

It forms a well-defined compound, NaI, $3\,C_3H6O_3$, which can be used for purifying it on the laboratory scale (J. C. S. 1913, **103**, 1255). With sodium or sodamide it forms the derivative $CH_3 \cdot C(ONa):CH_2$, and the higher ketones can be obtained by the action of sodamide and alkyl iodides on acetone or other ketones, thus diethyl ketone, sodamide, and methyl-iodide yield di-isopropyl ketone, $CHMe_2 \cdot CO \cdot CHMe_2$. (Ann. Chim. 1913, [viii], **29**, 213.) Acetone may be detected by the formation of indigo when its solution in sodium hydroxide is warmed with *o*-nitro-benzaldehyde.

Sulphonal, $(CH_3)_2:C(SO_2 \cdot C_2H_5)_2$, is formed when a mixture of acetone and mercaptan is treated with hydrochloric acid, and the **mercaptol,** $(CH_3)_2C(SC_2H_5)_2$, which is thus formed, is oxidized by potassium permanganate to the corresponding sulphone. It crystallizes in prisms, melts at 125°, and acts as a soporific.

Mesityl oxide, $C_6H_{10}O$, = $CH_3 \cdot CO \cdot CH:C(CH_3)_2$ (*Kane*, 1838; *Baeyer*), is a liquid of aromatic odour, boiling at 132°.

Phorone, $C_9H_{14}O$, = $(CH_3)_2C:CH \cdot CO \cdot CH:C(CH_3)_2$, forms readily fusible yellow crystals. Both compounds are obtained by saturating acetone with hydrochloric acid gas (A. **180**, 1).

Methyl ethyl ketone (2-*Butanone*), $CH_3 \cdot CO \cdot C_2H_5$, is present in crude wood spirit, and is also formed by the oxidation of secondary butyl alcohol. B.-pt. 81°.

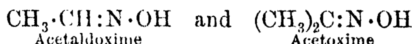
Pinacoline (2-*Dimethyl-3-butanone*), *methyl tertiary-butyl ketone*, $CH_3 \cdot CO \cdot C(CH_3)_3$, b.p. 106° is produced by the action of dilute sulphuric acid upon pinacone (p. 200). This involves a characteristic rearrangement, the "pinacoline reaction".

A number of ketones have been obtained from the higher fatty acids. These have been converted by *Krafft* into the corresponding paraffins, by first transforming them into the chlorides, $C_nH_{2n}Cl_2$, by means of PCl_5, and then heating the latter with hydriodic acid and phosphorus.

Both aldehydes and ketones appear to be isomerised to a certain extent into unsaturated alcohols under the influence of certain reagents, *e.g.* mineral acids, halogens, *Grignard* reagents, &c. cf. enolisation Chap. XLVII, G.

C. Aldoximes and Ketoximes

The aldoximes and ketoximes are the compounds obtained by the action of hydroxylamine on the aldehydes and ketones respectively. They both contain the bivalent oximino group $:N \cdot OH$ attached to carbon, *e.g.*:



$CH_3 \cdot CH:N \cdot OH$ (Acetaldoxime) and $(CH_3)_2C:N \cdot OH$ (Acetoxime)

They are either colourless crystalline compounds or liquids, and are both basic and acidic in properties. With metallic hydroxides they yield salts of the type $CH_3 \cdot CH:NOK$; with mineral acids they form salts in much the same manner as ammonia does, *e.g.* $CMe_2:NOH, HCl$.

The oximes are fairly readily hydrolysed by dilute acids, yielding hydroxylamine and either an aldehyde or a ketone.

On reduction they all yield primary amines, $:N \cdot OH \longrightarrow \cdot NH_2$.

Dehydrating agents, *e.g.* acetic anhydride or acetyl chloride, transform the aldoximes into nitriles, water being eliminated:



$$CH_3 \cdot CH:N \cdot OH = CH_3 \cdot C:N + H_2O.$$

The ketoximes with acetyl chloride followed by water undergo a rearrangement known as the *Beckmann transformation*, the final product being an acid amide or anilide.

Constitution.—In the formation of the oximes the water eliminated is undoubtedly formed from the oxygen of the carbonyl group and the hydrogen atoms of the hydroxylamine, otherwise the reaction would be of the type



$$CH_3 \cdot CO \cdot CH_3 + NH_2 \cdot OH = CH_3 \cdot CO \cdot CH_2 \cdot NH_2 + H_2O,$$

and an aminoketone would result. There are two possible ways in which water can be thus eliminated, yielding a compound $CMe_2{:}N \cdot OH$ or $CMe_2 \langle {}^{O}_{NH} \rangle$ (O and NH joined by a bond). That the first of these two formulæ is correct is demonstrated by the fact that when an alkyl derivative, $:C{:}N \cdot OR$ or $:C \langle {}^{O}_{N \cdot R} \rangle$ (O and N·R joined by a bond), is hydrolysed with hydrochloric acid an alkyl derivative of hydroxylamine, $NH_2 \cdot OR$, is obtained, and hence the alkyl group is presumably attached to oxygen in the alkylated oxime, and the oxime itself thus contains an OH group. This constitution formula is in perfect harmony with the reactions characteristic of oximes.

The oxime derived from an aldehyde or ketone often exists in isomeric forms. This is especially true of those derived from aromatic aldehydes and from mixed (unsymmetrical) ketones of the aromatic series. According to *Goldschmidt* and *V. Meyer*, these isomers are structurally identical, and are **stereo-isomeric** (*i.e.* the isomerism is due to the **spatial relationship** of the various atoms and radicals). See Chap. XLVI C.

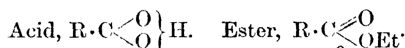
VI. MONOBASIC FATTY ACIDS

A. Saturated Acids, $C_nH_{2n}O_2$, or $C_nH_{2n+1} \cdot CO_2H$

The monobasic fatty acids are formed by the oxidation of the saturated primary alcohols or of their corresponding aldehydes. These acids are monobasic, *i.e.* contain in the molecule only one replaceable atom of hydrogen, since, as a rule, they give rise to only one series of salts or of esters. They are known as the **fatty acids**, because many

of them are contained in fats in the form of glyceryl esters.

The group characteristic of acids is the carboxylic group $\cdot C\!\lesssim^{O}_{O \cdot H}$, and it is the hydrogen of this group which becomes replaced in the formation of salts. The basicity of an acid depends on the number of such carboxylic groups present in the molecule. *Hantzsch* (B. 1917, **50**, 1422), in order to account for the different absorption spectra given by acids and their esters, suggests that in the acids and their salts the hydrogen or metal is attached to both oxygen atoms, but that in the esters the alkyl group is united to one oxygen only:



Acid, $R \cdot C\!\lesssim^{O}_{O}\}H$. Ester, $R \cdot C\!\lesssim^{O}_{OEt}$.

NORMAL FATTY ACIDS AND THEIR PHYSICAL DATA

		Melting-pt.	Boiling-pt.
Formic acid	CH_2O_2	8·3°	101°
Acetic acid	$C_2H_4O_2$	17°	118°
Propionic acid	$C_3H_6O_2$	− 36°	141°
Butyric acid	$C_4H_8O_2$	− 8°	162°
Valeric acid	$C_5H_{10}O_2$	...	186°
Caproic acid	$C_6H_{12}O_2$	+ 8°	205°
Heptoic acid	$C_7H_{14}O_2$	− 10°	224°
Caprylic acid	$C_8H_{16}O_2$	+ 16°	236°
Nonylic acid	$C_9H_{18}O_2$	12°	254°
Capric acid	$C_{10}H_{20}O_2$	31°	269°
Undecylic acid	$C_{11}H_{22}O_2$	29°	213°
Lauric acid	$C_{12}H_{24}O_2$	48°	226°
Tridecylic acid	$C_{13}H_{26}O_2$	51°	236°
Myristic acid	$C_{14}H_{28}O_2$	58°	248°
Pentadecylic acid	$C_{15}H_{30}O_2$	54°	257°
Palmitic acid	$C_{16}H_{32}O_2$	63°	269°
Margaric acid	$C_{17}H_{34}O_2$	60°	277°
Stearic acid	$C_{18}H_{36}O_2$	69°	287°
Nondecylic acid	$C_{19}H_{38}O_2$	66°	298°
Arachidic acid	$C_{20}H_{40}O_2$	75°	...
Behenic acid	$C_{22}H_{44}O_2$	83°	...
Lignoceric acid	$C_{24}H_{48}O_2$	80°	...
Cerotic acid	$C_{26}H_{52}O_2$	78°	...
Melissic acid	$C_{30}H_{60}O_2$	90°	...

The lower members of the series are liquids of pungent

odour and corrosive action, and boil without decomposition. They dissolve readily in water, and the aqueous solutions exhibit a strongly acid reaction, although most of the anhydrous acids are without action on dry litmus paper. The intermediate members have an unpleasant smell like that of rancid butter or perspiration, and are oily and but slightly soluble in water. Mobility, odour, and solubility diminish as the percentage of carbon increases. The higher members, from C_{10}, are solids, like paraffin, insoluble in water, and can only be distilled without decomposition in a vacuum. Their acid character no longer finds expression in their reaction with litmus, but in their capability of forming salts with bases. These higher acids are readily soluble in alcohol, and especially in ether.

In this series the boiling-point rises regularly for each increase in the number of C atoms in the molecule. The rise is roughly 19° for each increment of CH_2. The melting-points do not exhibit the same regularity: the melting-point of any acid containing an even number of C atoms in the molecule is higher than the melting-point of the acid with an odd number of C atoms which immediately succeeds it.

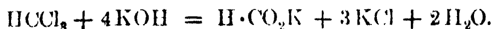
Similar phenomena have been observed in other homologous series. (See chapter on Physical Properties and Constitution, XLVII.)

The specific gravity of the liquid acids is at first > 1, and from C_3 onwards < 1, and it decreases continuously to about 0·8, the paraffin character of the hydrocarbon radical becoming preponderant.

Occurrence.—Many of the acids of this series are found in nature in the free state, but more frequently as esters, viz.:—(*a*) esters of monohydric alcohols (see wax varieties), (*b*) esters of glycerol or glycerides, in most of the vegetable and animal fats and oils. For further particulars see pp. 163 and 164.

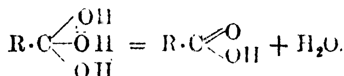
Formation.—1. By the oxidation of the primary alcohols, $R\cdot CH_2\cdot OH$, or their aldehydes, $R\cdot C\!\begin{smallmatrix}\diagup H\\ \diagdown\!\!\diagdown O\end{smallmatrix}$, by means of $K_2Cr_2O_7$ or MnO_2 and dilute H_2SO_4, or by the oxygen of the air in presence of platinum or of nitrogenous substances, *e.g.* acetic acid from alcohol. The acids thus formed contain the same number of carbon atoms as the alcohol or aldehyde. Many complex carbon compounds, *e.g.* ketones, unsaturated compounds, &c., when oxidized yield acids containing a smaller number of carbon atoms. The higher acids of this series are converted into their lower homologues when oxidized.

2. Several acids have been prepared from the halogen compounds containing the group $\cdot CX_3$, *e.g.*:—



$$HCCl_3 + 4KOH = H\cdot CO_2K + 3KCl + 2H_2O.$$

We should expect an exchange of the three chlorine atoms for three hydroxyls, with formation of the intermediate compounds $CH(OH)_3$ or $R\cdot C(OH)_3$. Such compounds are, however, extremely unstable, and immediately eliminate water, yielding the acids (cf. p. 131):

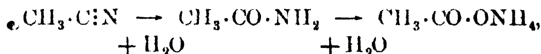


$$R\cdot C\begin{cases}OH\\OH\\OH\end{cases} = R\cdot C\begin{cases}O\\OH\end{cases} + H_2O.$$

But derivatives of these trihydric alcohols, or **ortho-acids** as they are termed, are known; for example, **ethyl ortho-formate,** $HC(OC_2H_5)_3$, a neutral liquid of aromatic odour, insoluble in water, and boiling at 146°.

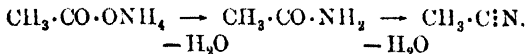
3. From the alkyl cyanides or nitriles, $C_nH_{2n+1}CN$. The cyanides, which are prepared by warming the alkyl iodides with cyanide of potassium, are converted into the fatty acids and ammonia by hydrolysis with potassium hydroxide solution, with dilute or concentrated hydrochloric acid, or with sulphuric acid diluted with its own volume of water.

The reaction may be regarded as the addition of two molecules of water to each molecule of nitrile:



$$CH_3\cdot C{:}N \underset{+H_2O}{\longrightarrow} CH_3\cdot CO\cdot NH_2 \underset{+H_2O}{\longrightarrow} CH_3\cdot CO\cdot ONH_4,$$

first yielding the acid **amide,** and then the ammonium salt of the acid, which is decomposed by the hydrolysing agent employed. The process, in the case of aromatic nitriles, can be stopped at the point when the acid amide is formed, but in the aliphatic series this is almost impracticable. The reaction is the exact reverse of the formation of nitriles from the ammonium salts of fatty acids:



$$CH_3\cdot CO\cdot ONH_4 \underset{-H_2O}{\longrightarrow} CH_3\cdot CO\cdot NH_2 \underset{-H_2O}{\longrightarrow} CH_3\cdot C{:}N.$$

The great importance of this reaction, by means of which we can obtain an acid C_{n+1} from an alcohol C_n, has been already indicated (p. 105). And since the acids can be converted indirectly by reduction into the corresponding alcohols,

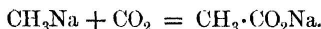
it is thus possible to build up synthetically, step by step, the alcohols richer in carbon from those poorer in carbon, a circumstance which is of especial importance in the case of the normal alcohols (*Lieben* and *Rossi*). As an example:



$$CH_3{\cdot}OH \xrightarrow[\text{P and I}]{} CH_3I \xrightarrow[\text{KCN}]{} CH_3{\cdot}CN \xrightarrow[\text{Hydrolysis.}]{} CH_3{\cdot}COOH.$$

The acid may be converted into the alcohol containing the same number of carbon atoms by one of the following methods: (*a*) Ca salt + Ca formate ⟶ aldehyde ⟶ alcohol; (*b*) acid chloride reduced gives alcohol; (*c*) ethyl ester reduced gives alcohol.

4. The direct introduction of the carboxylic group into a paraffin can be accomplished by the action of carbon dioxide on the sodium alkyl compound at a suitable temperature (*Wanklyn*):



$$CH_3Na + CO_2 = CH_3{\cdot}CO_2Na.$$

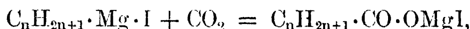
Formic acid is obtained from hydrogen and carbon dioxide, under the influence of the silent electric discharge:



$$H_2 + CO_2 = H{\cdot}CO_2H;$$

or from hydrogen, potassium, and carbon dioxide, when the potassium is placed in a bell-jar filled with moist carbon dioxide (*Kolbe* and *Schmitt*, 1861); or by treating carbonate of ammonia, &c., with sodium amalgam.

5. By the action of carbon dioxide on ethereal solutions of organo-magnesium haloids, a magnesium compound,



$$C_nH_{2n+1}{\cdot}Mg{\cdot}I + CO_2 = C_nH_{2n+1}{\cdot}CO{\cdot}OMgI,$$

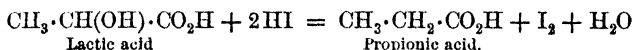
is obtained, which gives the free acid on the addition of dilute sulphuric acid (C. 1904, **138**, 1048).

6. By passing carbon monoxide over heated alkali alcoholate; from the alcohol and CO over heated CuO or Cu, or even from an alcohol and CO under pressure at 300–400° with an acid catalyst, *e.g.* phosphoric acid, $CH_3{\cdot}ONa + CO = CH_3{\cdot}CO_2Na$ (at 160°).

7. By the addition of hydrogen to unsaturated acids, *e.g.* propionic acid, $CH_3{\cdot}CH_2{\cdot}CO_2{\cdot}H$, from acrylic acid, $CH_2{:}CH{\cdot}CO_2H$. This addition of hydrogen may be effected (*a*) directly by hydriodic acid and phosphorus, sodium amalgam and water, or by the aid of hydrogen and reduced nickel at a temperature of about 100° (Abstr. 1903, **1**, 547), or hydrogen and colloidal

palladium at the ordinary temperature, Chap. XLIV C; (*b*) indirectly, by addition of hydrobromic acid and inverse substitution. Unsaturated acids also yield saturated ones containing fewer carbon atoms when fused with potash, *e.g.* 1 mol crotonic acid, $C_4H_6O_2$, yields 2 mols. acetic acid, $C_2H_4O_2$.

8. From the hydroxy acids, by reduction with hydriodic acid:



$$\underset{\text{Lactic acid}}{CH_3 \cdot CH(OH) \cdot CO_2H} + 2HI = \underset{\text{Propionic acid.}}{CH_3 \cdot CH_2 \cdot CO_2H} + I_2 + H_2O$$

9. From many polybasic acids, by the elimination of CO_2, for example, formic from oxalic, $COOH \cdot COOH$, and acetic from malonic, $CO_2H \cdot CH_2 \cdot CO_2H$.

10. *Aceto-acetic ester syntheses.*—The homologues



$$R \cdot CH_2 \cdot COOH \text{ and } {}^{R}_{R'}\!\!>CH \cdot COOH$$

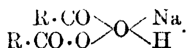
can be prepared from acetic acid by first converting the latter into aceto-acetic ester, $CH_3 \cdot CO \cdot CH_2 \cdot COOC_2H_5$, introducing alkyl groups into this, and then decomposing the compound so obtained by concentrated alcoholic potash. (Cf. Aceto-acetic Ester, p. 236; and Malonic Ester, p. 245.)

Separation.—Natural fats are nearly all glycerides, *i.e.* esters derived from the trihydric alcohol, glycerol, and various fatty and other acids, so that a mixture of acids is obtained when any natural fat is hydrolysed. This mixture may be separated into its components as follows:—

(*a*) By fractional distillation in a good vacuum; (*b*) by fractional precipitation of an alcoholic solution of the acids by means of magnesium acetate, calcium chloride, &c., the acids richer in carbon being precipitated first; (*c*) by fractional solution: the dry barium salts of formic, acetic, propionic, and butyric acids are very differently soluble in alcohol, the solubility increasing rapidly with the number of carbon atoms; (*d*) by fractional neutralization, and distillation of the non-combined acid.

Behaviour.—1. *Salts.* The acids are monobasic, and thus form **normal salts**, *e.g.* $CH_3 \cdot CO_2Na$. They also yield **acid salts**—the so-called **per-acid salts**—from the existence of which we might feel inclined to doubt their monobasic nature. These salts can, however, be crystallized from a strongly acid solution only; they decompose on the addition of water, and also lose their excess of acid when heated. The formation of

such acid salts is now usually regarded as being due to the quadravalency of one of the oxygen atoms, *e.g.*:



All the other chemical characteristics of the acids go to prove their monobasicity, especially the non-formation of acid esters.

2. The monobasic acids give rise to different groups of derivatives in much the same manner as the monohydric alcohols. The typical hydrogen atom is replaceable by an alkyl group with formation of an **ester or alkyl salt**, *e.g.* $CH_3 \cdot CO \cdot OC_2H_5$, ethyl acetate, or by a second acid radical with formation of an **anhydride**; the hydroxyl may further be replaced by halogen, especially chlorine, to an **acid chloride**, by SH to a **thio-acid**, by NH_2 to an **amide**, &c. (See Acid Derivatives, p. 177.)

3. Halogens act upon the acids as substituents (see p. 173).

4. When the alkali salts are heated with soda lime, or frequently when the silver salts are heated alone, carbon dioxide is eliminated and a paraffin formed (see *e.g.* Methane). Paraffins are also formed when the alkali salts are electrolysed (see Ethane)

5. Most of the acids are relatively stable towards oxidizing agents, formic acid alone being readily oxidized to carbonic acid, and thus possessing strong reducing properties.

6. When the lime salts of the acids are heated with calcium formate they are reduced to aldehydes, and when heated for a lengthened period with hydriodic acid and phosphorus, to paraffins.

6*a*. When the lime salts are distilled alone, or when the higher acids are heated with phosphorus pentoxide, they are transformed into the ketones, $(C_{n-1}H_{2n-1})_2CO$.

Constitution.—It follows from their modes of formation, especially 3, 4, and 6, and also from their behaviour (see 4 above), that acetic acid and its higher homologues contain alkyl radicals. The conversion of the alcohols into acids containing 1 atom of carbon more, by means of the cyanides, is especially strong proof of this. The latter contain the alkyl radical bound to the nitrile group $\cdot C \vdots N$, and when they are hydrolysed the alkyl radical remains unchanged, and the tervalent nitrogen is replaced by O'' and $(OH)'$, both of these attaching themselves to the carbon atom of the original cyanogen, and so forming the group



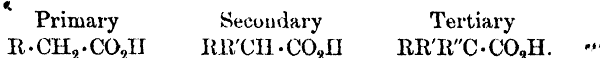
Consequently all the oxygen in the acid is united to a single carbon atom in the form of the group CO_2H. This group, which is termed carboxyl, is characteristic of the existence of acid properties. Further proof of the presence of the carboxyl group is based largely on the reactions of the acids. The alkyl group which they contain must be directly attached to C, as it is not removed by the action of acids or alkalis. We thus have $C_nH_{2n+1}\cdot C$. The presence of an OH group follows from the reaction of the acids with PCl_3 or PCl_5, when an atom of O and an atom of H become replaced by an atom of Cl, and they must presumably therefore be present in the form of the univalent $\cdot O\cdot H$ group. There is only 1 oxygen atom left over to account for, and this is presumably attached to the C by a double bond, and thus we have $C_nH_{2n+1}\cdot C\begin{matrix}\nearrow O \\ \searrow OH\end{matrix}$. The monobasic acids may therefore be regarded as compounds of the alkyl radicals with carboxyl, or, in other words, as derived from paraffins by the replacement of one hydrogen atom by a carboxyl group, thus:—



$$C_{n-1}H_{2n-1}\cdot CO_2H = C_nH_{2n}O_2.$$

Formic acid is, in this way, the hydrogen compound of carboxyl, $H\cdot CO_2H$.

The acids are distinguished as *primary*, *secondary*, or *tertiary*, according as the alkyl radicals which they contain are primary, &c. Thus:—



Primary	Secondary	Tertiary
$R\cdot CH_2\cdot CO_2H$	$RR'CH\cdot CO_2H$	$RR'R''C\cdot CO_2H$.

There is no room for doubt that it is the hydrogen atom of the carboxyl group, the so-called "typical" hydrogen atom, which is replaced by metals in the formation of salts, for the foregoing acids are all monobasic, and consequently the number of hydrogen atoms present in the alkyl radical is of no moment for the acid character. In the di- and polybasic acids, the presence of two or more carboxyls can usually be demonstrated.

If the composition of the primary alcohols, $R\cdot CH_2\cdot OH$, is compared with that of the corresponding acids, $R\cdot CO\cdot OH$ (R = alkyl or hydrogen), the latter are seen to be derived from the former by the exchange of two atoms of hydrogen for one atom of oxygen. The character of the original

substance is thus completely changed by the entrance of the electro-negative (acidifying) oxygen.

Nomenclature.—The names for the first five acids are special; from C_6 onwards, with a few exceptions, the names for the *normal* acids indicate the number of carbon atoms, *e.g.* hexoic, heptoic, or heptylic, &c. The systematic name (Geneva Congress) of the normal compound is obtained by adding the word acid to the name of the paraffin containing the same number of carbon atoms, *e.g.* acetic acid = ethane acid.

The monovalent radicals left when OH is removed from the molecule of each acid are often spoken of as acid or acyl radicals. (Cf. Alkyl Radicals.) The commonest of these radicals are $CH_3 \cdot CO \cdot$, acetyl; $C_2H_5 \cdot CO \cdot$, propionyl; $C_3H_7 \cdot CO \cdot$, butyryl; &c.

The aldehydes may be looked upon as hydrogen compounds of the acyl radicals, and the ketones as compounds of the latter with alkyl radicals, thus:—


$(CH_3 \cdot CO)H$ (aldehyde) $(CH_3 \cdot CO)CH_3$ (acetone).

The constitution of aldehydes and ketones, and of compounds derived from them, is based on the constitution of the monobasic acids.

Isomers.—The acids of the acetic series show the same isomerism as the alcohols containing 1 atom of carbon less, since they are formed from these by means of the cyanides. Thus we have 1 propionic acid, 2 butyric acids corresponding with the 2 propyl alcohols, 4 valeric acids corresponding with the 4 butyl alcohols, and so on.

Formic acid (*Methane acid*), *acidum formicicum*, CH_2O_2 (*Samuel Fisher* and *John Wray*, 1670; *Marggraf*), occurs free in ants, especially *Formica rufa*, in the processionary caterpillar (*Bombyx processionea*), in the bristles of the stinging nettle, the fruit of the soap-tree (*Sapindus saponaria*); also in small quantity in perspiration, urine, and the juice of flesh.

Formation.—From HCN, $CHCl_3$, CH_2OH, CO_2, &c. (See General Methods of Formation.) Its salts are obtained by the reducing action of sodium amalgam upon ammonium carbonate or solutions of the alkali hydrogen carbonates (*Lieben*); the free acid by the dry distillation or oxidation of many organic substances, *e.g.* starch (*Scheele*).

Preparation.—1. Sodium formate is manufactured by absorbing carbon monoxide in soda lime at 210° (*Merz*). For kinetics of the reaction, see *Bredig*, Z. Elec. 1914, **20**, 489.

2. When oxalic acid is heated, formic acid is obtained in small quantity together with carbon monoxide, carbon dioxide, and water, and the same effect is produced by the direct action of sunlight upon its aqueous solution containing uranic oxide:



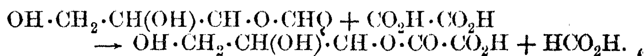
$$C_2H_2O_4 = CO_2 + CH_2O_2.$$

This decomposition is best effected by heating crystallized oxalic acid with glycerol to 100°–110° (*Berthelot, Lorin*), and adding more oxalic acid crystals as soon as the evolution of carbon dioxide ceases. The reaction can be repeated a number of times, and relatively large amounts of formic acid are produced from oxalic acid by the use of a relatively small amount of glycerol. The first product is a mon-oxalate of glycerol,



$$OH{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2{\cdot}O{\cdot}CO{\cdot}CO_2{\cdot}H,$$

which then decomposes into CO_2 and **glyceryl monoformate** or **monoformin,** $OH{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2{\cdot}O{\cdot}CHO$ (cf. glyceryl esters). The addition of more oxalic acid liberates formic acids, and this distils over with the water from the crystals added, and glyceryl monoxalate is reformed. (*Chattaway*, J. C. S. 1914, **105**, 151.)



$$OH{\cdot}CH_2{\cdot}CH(OH){\cdot}CH{\cdot}O{\cdot}CHO + CO_2H{\cdot}CO_2H$$
$$\longrightarrow OH{\cdot}CH_2{\cdot}CH(OH){\cdot}CH{\cdot}O{\cdot}CO{\cdot}CO_2H + HCO_2H.$$

The anhydrous acid is obtained by decomposing the solid lead or copper salt with sulphuretted hydrogen.

Properties.—It is a colourless liquid which solidifies in the cold and fumes slightly in the air. M.-pt. + 9°; b.-pt. 101°; sp. gr. 1·22. It has a pungent acid and ant-like odour, acts as a powerful corrosive, and produces sores on the soft parts of the skin. It is a much stronger acid than acetic acid, is a powerful antiseptic, and decomposes completely into carbon monoxide and water when heated with concentrated sulphuric acid: $CH_2O_2 = CO + H_2O$.

Salts.—**Potassium-**, HCO_2K, **sodium-**, HCO_2Na, and **ammonium formate,** HCO_2NH_4, form deliquescent crystals. The first two yield oxalates when strongly heated, with evolution of hydrogen (see Oxalates); the ammonium salt yields formamide and water at 180°:



$$HCO_2{\cdot}NH_4 = H{\cdot}CO{\cdot}NH_2 + H_2O.$$

The lead salt, $Pb(HCO_2)_2$, forms glistening, sparingly soluble needles, the **copper** salt, $Cu(HCO_2)_2 + 4H_2O$, large blue monoclinic crystals, and the **silver** salt colourless crystals. The last-mentioned deposits silver when warmed, consequently a solution of nitrate of silver is reduced when heated with formic acid.

A solution of the soluble **mercuric** salt, $Hg(HCO_2)_2$, evolves carbon dioxide when gently warmed, and yields free formic acid together with the sparingly soluble **mercurous** salt, $Hg_2(HCO_2)_2$, which separates in white plates; on further heating, carbon dioxide, formic acid, and metallic mercury are obtained. Similarly an aqueous solution of mercuric chloride is reduced by formic acid to the mercurous salt, Hg_2Cl_2.

Formic acid is thus a strong reducing agent, and in this respect differs from the other members of the series:



$$HCO \cdot OH = CO_2 + 2H.$$

It decomposes into carbonic acid and hydrogen when heated alone to 160°, or when brought into contact with finely-divided rhodium.

This power of reduction may be attributed to the aldehydic grouping contained in its constitutional formula, $H \cdot O \cdot CH:O$.

Acetic acid (*Ethane acid*), $CH_3 \cdot COOH$, was known in the dilute form, as crude wine vinegar, to the ancients. *Stahl* prepared the concentrated acid about 1700. *Glauber* mentions wood vinegar (1648). Its constitution was established by *Berzelius* in 1814. Salts of acetic acid are found in various plant juices, especially those of trees, and in the perspiration, milk, muscles, and excrementa of animals. Esters of acetic acid also occur, *e.g.* triacetin in croton-oil (see p. 164, and also under Glycerol).

Formation (see p. 147 *et seq.*).—It is the final product of the oxidation of a great many compounds, and also of their treatment with alkalis.

The following synthesis is of historical interest:—Perchloroethylene, C_2Cl_4, which is prepared from CCl_4, *i.e.* from Cl and CS_2, yields with chlorine in presence of water in direct sunlight trichloracetic acid, carbon hexachloride, C_2Cl_6, being obviously formed as intermediate product (*Kolbe*, 1843):



$$CCl_3 \cdot CCl_3 + 2H_2O = CCl_3 \cdot CO_2H + 3HCl.$$

The latter acid is reduced to acetic by nascent hydrogen (*Melsens*).

Preparation.—1. *From alcohol.*—A dilute aqueous solution of alcohol, containing up to 15 per cent, is slowly converted into acetic acid on exposure to the oxidizing action of the air and in presence of certain low forms of plant life known as bacteria, especially *Bacterium aceti.* These organisms are contained in the air, and hence become deposited in alcoholic liquors exposed to the air, and thus produce the souring of wines, &c. For the growth of the micro-organisms it is essential that nitrogenous matter, phosphates, &c., shall be present, and hence pure alcohol mixed with water does not turn sour. In the "quick process" dilute alcoholic liquors are allowed to trickle over beechwood shavings which have been previously coated with the required bacteria (mother of vinegar), and the temperature is kept at about 35°.

Vinegar is an aqueous solution of acetic acid, usually containing only 3 to 5 per cent, but containing also small quantities of alcohol, of the higher acids, *e.g.* tartaric and succinic, the ethyl esters of the acids, albuminoid matters, &c.

2. *From wood.*—The dry distillation of wood, which is conducted in cast-iron retorts, yields: (1) gases, *e.g.* hydrogen 15 per cent, methane 11 per cent, carbon dioxide 26 per cent, carbon monoxide 41 per cent, and higher hydrocarbons 7 per cent; (2) an aqueous solution known as pyroligneous acid, which, in addition to acetic acid, contains methyl alcohol, acetone, homologues of acetic acid, and strongly smelling combustible products (empyreuma); and (3) wood-tar, which contains compounds of the nature of carbolic acid. The pyroligneous acid is worked up for acetic acid by converting it into the sodium or calcium salt, heating these—the former to fusion, and the latter to 200°, and then distilling with sulphuric acid.

3. For its formation from acetylene, cf. Chap. L, G.

Properties.—Acetic acid is a strongly acid liquid of pungent odour, which feels slippery to the touch and burns the skin, and which solidifies on a cold day to large crystalline plates melting at 17°; (glacial acetic acid). It boils at 118°, and its vapour burns with a blue flame; sp. gr. at 15° = 1·055. When mixed with water, contraction and consequent increase in density ensue, the maximum point corresponding with the hydrate $CH_3{\cdot}CO_2H + H_2O$, = $CH_3{\cdot}C(OH)_3$ (ortho-acetic acid), which contains 77 per cent acid and has a sp. gr. of 1·075 at 15·5°; after this, the specific gravity decreases with further addition

of water, so that a 50-per-cent acid has almost the same density as one of 100 per cent. The amount of acid present in a solution is determined either by its sp. gr., this contraction being borne in mind, or by titration with standard alkali, using phenolphthalein as indicator, or with very concentrated acid by a careful determination of its melting- (freezing-) point in the *Beckmann* apparatus. The vapour density near the boiling-point is much higher than that required by theory, but is normal above 250°. The high values are due to the association of the molecules at the lower temperatures, and in the liquid state the molecular formula is undoubtedly $(C_2H_4O_2)_2$, &c. The acid is hygroscopic, and stable towards chromic acid and cold permanganate of potash. It dissolves phosphorus, sulphur, and many organic compounds, is corrosive, and gives rise to painful wounds on tender parts of the skin.

Salts.—All the normal acetates are soluble in water. The following **potassium** salts are known:—(*a*) $KC_2H_3O_2$, (*b*) $KC_2H_3O_2$, $HC_2H_3O_2$, and (*c*) $KC_2H_3O_2$, $2\,HC_2H_3O_2$.

Sodium acetate, $CH_3\cdot COONa$, $3\,H_2O$, forms transparent readily soluble rhombic prisms. **Ammonium acetate,** $CH_3\cdot CO\cdot ONH_4$, resembles the potassium salt. It is used in medicine as a sudorific (liquor ammonii acetici). Its solution loses ammonia on evaporation, and it yields acetamide when distilled. **Ferrous acetate,** $Fe(C_2H_3O_2)_2$, is largely used in the form of "iron liquor" as a mordant in dyeing. The normal **ferric** salt, $Fe(C_2H_3O_2)_3$, which is employed for the same purpose, is obtained when a soluble ferric salt is mixed with sodium acetate. Its solution is deep red in colour, and deposits the iron as **basic salt,** $CH_3\cdot CO\cdot OFe(OH)_2$, when heated with excess of water. It is used in medicine as "liquor ferri acetici". The analogous **aluminic acetate** is known only in solution, and finds a wide application as "red liquor" mordant in calico printing and dyeing. Its use depends upon the fact that it is readily hydrolysed by water, *e.g.* when exposed to the action of steam, and on the insolubility of the compound (lake) formed from the residual alumina and the colouring matter. It is employed in small doses as an astringent in cases of diarrhœa, &c. Lead salts. (1) **Normal lead acetate** or sugar of lead, $(CH_3\cdot COO)_2Pb + 3\,H_2O$, is manufactured from sheet-lead and acetic acid. It forms colourless lustrous four-sided prisms, which are poisonous and of a nauseous sweet taste. It combines with lead oxide to (2) **basic salts** of alkaline reaction, termed sub-acetates.

The simplest basic salt has the composition $OH \cdot Pb \cdot O \cdot CO \cdot CH_3$, but there also exist others, *e.g.* $OH \cdot Pb \cdot O \cdot Pb \cdot O \cdot CO \cdot CH_3$, &c. Two molecules of acetic acid can combine with as many as 5 molecules of lead oxide. These basic acetates are used as *Goulard's* lotion, and on the large scale for the preparation of white lead, &c.

Cupric acetate, $Cu(C_2H_3O_2)_2 + 2H_2O$, dark-green crystals, also forms basic salts (verdigris). **Silver acetate**, $AgC_2H_3O_2$, forms characteristic glistening needles.

Detection of Acetic Acid.—(1) When an acetate is heated with alcohol and sulphuric acid, the pleasant-smelling ethyl acetate is formed; (2) by means of the silver salt; (3) by the odour of cacodyl produced upon heating the potassium or sodium salt with arsenious oxide. (See p. 120.)

Propionic acid, $CH_3 \cdot CH_2 \cdot CO_2H$ (*Gottlieb*, 1844), may be obtained by the reduction of acrylic or lactic acid (see pp. 149 and 150); also from lactate or malate of calcium by suitable *Schizomycetes* fermentation (*Fitz*). It is usually prepared by the oxidation of propyl alcohol with dichromate mixture. (See p. 147.)

Calcium chloride separates it from its aqueous solution in the form of an oil, whence its name πρῶτος, the first, and πίων, fat; the first oily acid.

Butyric acids, $C_4H_8O_2$.

1. **Normal butyric acid**, *butane acid, ethylacetic acid*, $CH_3 \cdot CH_2 \cdot CH_2 \cdot CO_2H$, occurs free in perspiration, in the juice of flesh, in the contents of the large intestine, and in the solid excrementa; as hexyl ester in the oil of the fruit of *Heracleum giganteum*, as octyl ester in *Pastinaca sativa*, and to the extent of 2 per cent as glyceride in butter (*Chevreul*, 1822).

Formation.—(See also General Modes of Formation.) It is produced (1) by the decay of moist fibrin and of cheese (being therefore contained in Limburg cheese); (2) by a *Schizomycetes* fermentation of glycerol, and of carbohydrates (*Pelouze* and *Gélis*; *Fitz*; see below); (3) by the oxidation of albuminoids with chromic acid, of fats with nitric acid, of coniine, &c., and (4) by the dry distillation of wood.

Preparation.—In the "butyric fermentation" of sugar or starch by fission ferments (*e.g. Bacillus butylicus*), $CaCO_3$ or ZnO being added at the same time, to neutralize the acid formed.

If the fermentation is brought about by impure material

(decaying cheese, &c.), lactic acid is first produced by other micro-organisms, this being then converted into butyric acid by the butyric bacillus.

Properties.—It is a thick liquid of unpleasant rancid odour, in presence of ammonia like that of perspiration, is miscible with water, and separates from its aqueous solution on the addition of salts. B.-pt. 163°. The calcium salt, $Ca(C_4H_7O_2)_2 + H_2O$, forms glistening plates, and is characterized by being more soluble in cold than in hot water; it therefore separates on warming the concentrated cold aqueous solution. On prolonged heating of the solution, however, it is transformed into the calcium salt of isobutyric acid.

2. **Isobutyric acid,** *2-methyl-propane acid, dimethyl-acetic acid,* $(CH_3)_2:CH\cdot CO_2H$, is present in the free state in the carob (*Redtenbacher*), in the root of *Arnica montana*, and as esters in *Pastinaca sativa* and Roman chamomile oil.

It is obtained from isopropyl cyanide (*Erlenmeyer*), by the oxidation of isobutyl alcohol, by the aceto-acetic ester synthesis (p. 236), &c. It resembles *n*-butyric acid, but is more sparingly soluble in water (1 in 5), and boils 9° lower, *i.e.* at 154°. Unlike the latter, however, it is easily oxidized to acetone or acetic acid, and carbonic acid. The calcium salt, $Ca(C_4H_7O_2)_2$, differs from its isomer in being more soluble in hot water than in cold. The solution is accompanied by a slight absorption of heat, whereas the solution of the salt of the *n*-acid is accompanied by a slight evolution of heat.

Valeric acid, $C_5H_{10}O_2$, exists in the four different modifications which are theoretically possible:

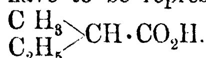
1. **Normal Valeric acid** (*Pentane acid*), *propyl-acetic acid,* $CH_3\cdot(CH_2)_3\cdot CO_2H$, from normal butyl cyanide (*Lieben* and *Rossi*, 1871), is best prepared from propyl-malonic acid. (See B. **21**, Ref. 649; also malonic ester synthesis.) It boils at 185°, and is soluble in 27 parts of water.

2. **Isovaleric acid,** *3-methyl-butane acid, isopropyl-acetic acid,* $(CH_3)_2:CH\cdot CH_2\cdot CO_2H$, is obtained from isobutyl cyanide. It is found in the free state and in the form of esters in the animal kingdom and in many plants, especially (free) in the valerian root (*Valeriana officinalis*), and in the angelica root (*Angelica archangelica*), from which it is obtained by boiling with soda; further, in the blubber of the dolphin (*Chevreul*, 1817), in the berries of *Viburnum opulus*, in the perspiration from the foot, &c. The natural acid is usually mixed with the active valeric acid, and is therefore optically

active; the oxidation of fermentation amyl alcohol by chromic acids yields a similar mixture. When pure it is optically in active, boils at 175°, and has an unpleasant pungent acid odour, like that of old cheese, and a corrosive action. It is used in medicine.

3. **Methyl-ethyl-acetic acid**, *active valeric acid*, *2-methyl-butane acid*, $\begin{matrix} CH_3 \\ C_2H_5 \end{matrix}{>}CH \cdot CO_2H$, occurs in nature, as already mentioned, and results from the oxidation of the active (−) amyl alcohol; it is in this case (+) optically active, while, if prepared synthetically, *e.g.* by the aceto-acetic ester reaction, it is optically inactive, but can be resolved by suitable methods into a + valeric acid and a − valeric acid. [For determination of optical activity, see Section on Physical Properties.]

There are thus three distinct acids, one dextro-rotatory, one lævo-rotatory, and the third optically inactive, which have to be represented by the same structural formula, viz.,

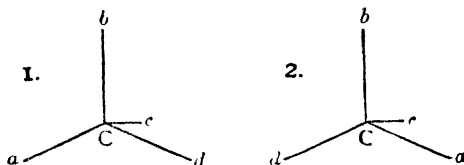


$\begin{matrix} CH_3 \\ C_2H_5 \end{matrix}{>}CH \cdot CO_2H.$

As regards their ordinary chemical and physical properties, the two active acids are exactly alike, and differ only in their action on polarized light. This difference is not due to the different arrangements of the molecules, as all three are liquids, and in liquids the molecules are not usually regarded as having definite arrangements. A further proof that the cause of the activity, and hence of the isomerism, is to be sought for in the molecules themselves, and not in any special arrangements of the molecules, is the fact that the optical properties of the acids in the gaseous state are similar to those in the liquid. The investigations of *Pasteur*, *Le Bel*, and *Van't Hoff* have shown that this kind of isomerism, which is now usually termed **stereo-isomerism**, is due to the fact that the compound contains a carbon atom to which 4 different radicals are attached; in the case of valeric acid these are, H, CH_3, C_2H_5, CO_2H. Such a carbon atom is usually termed an asymmetric carbon atom. (This expression does not mean that the carbon atom itself is asymmetric in shape, but that it is attached to four distinct radicals, and as we shall see later this produces an asymmetric molecule.)

Van't Hoff showed that if we assume that these radicals are arranged around the carbon atom, not in a single plane, but in the three dimensions of space, then every compound con-

taining a single asymmetric carbon atom should exist in the modifications represented by the figures 1 and 2.

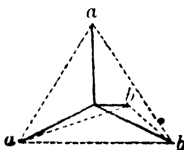


Such modifications are not identical, since they cannot be brought to superposition (this can be shown readily by the aid of models), but they are very similar; in fact, they stand in the relationship of the right to the left hand, or in the relationship of an asymmetric object to its mirror image. They are enantimorphous.

The spatial relationship of the radicals is often expressed by stating that if the asymmetric carbon atom is situated as the centre of a regular tetrahedron, then the four radicals occupy the solid angles of the tetrahedron. The arguments in favour of the spatial representation of the molecules of carbon compounds are largely based on a consideration of the number of isomeric forms in which simple carbon derivatives occur. For example, no simple compound of the type C a a b b is known to exist in more than one modification. If, however, the radicals and carbon atom were arranged in a single plane, we should expect the two modifications:



but with the spatial or tetrahedral arrangement we can get but the one modification.



An examination of models* will clearly show that in whatever way we exchange the radicals *a* and *b*, we always arrive at a figure which can be superimposed on the one depicted.

Similarly with regard to compounds C a a b c, in which 2 of the 4 radicals are alike. The tetrahedral arrangement allows of one modification only, and in these cases only one is actually known. When, however, all four radicals are distinct, *e.g.* C a b c d, the spatial arrangement admits of two enantiomorphous or non-superposable **configurations**, which are in the relationship of object to mirror image, and these two modifications represent the two optically active isomerides. in which almost every compound of the type C a b c d has been shown to exist. An examination of the models representing the two modifications shows that they are both asymmetric, *i.e.* a plane of symmetry cannot be drawn through them, and the optical activity which such compounds exhibit when in the liquid state, or in solution, is undoubtedly connected with the asymmetry of their molecules. Since the two configurations contain the same radicals and are very similar, in the one case containing the 4 radicals arranged in what we may term a positive, and in the other, in the opposite or negative direction, we should expect the molecules of the two compounds to produce rotations of the polarized ray equal in magnitude but of opposite sign. This is the case with the two optically active valeric acids: the pure dextro-acid has a rotation of $+ 17{\cdot}85^\circ$, and the lævo-acid $- 17{\cdot}85^\circ$.

In addition to the two optically active modifications, a third isomeride is usually known which is optically inactive. As it can be synthesised by mixing together equal weights of the *d* and *l* compounds, it follows that such a compound is either a mixture or a definite compound of the two active isomerides, *i.e.* its optical inactivity is owing to the fact that the two components are present in equal quantities. Such isomerides are often spoken of as **racemic compounds, and are optically inactive by external compensation.** Such racemic compounds may be resolved into their optically active components by

* In using models it must be remembered that the models are not supposed to represent in the least the actual shapes of the atoms, but merely their spatial relationships. It must also be borne in mind that the atoms and radicals in the molecules are in a state of motion, and the fixed position represented in the model may be supposed to represent the mean position of the centre of gravity of any particular atom in its oscillatory motion, or the position which the centre of gravity would occupy at absolute zero.

several methods, most of which were devised by *Pasteur*. (See Racemic Acid.)

Relationship between Dissymmetry of the Molecule and Optical Activity.—Since the two isomerides of the type C a b c d are optically active, it should follow that any derivative of valeric acid in which the four radicals attached to the central carbon atom are still different should be also optically active, but that a derivative in which two of the radicals become similar should become inactive. This question has been examined by *Le Bel* in the case of some forty derivatives of active amyl alcohol, $\begin{matrix} CH_3 \\ C_2H_5 \end{matrix} > C < \begin{matrix} H \\ CH_2OH \end{matrix}$. The alcohol, its chloride, amine, all its esters, its oxidation product, viz. valeric acid, and all its salts, esters, &c., are optically active; the hydrocarbon $\begin{matrix} CH_3 \\ C_2H_5 \end{matrix} > C < \begin{matrix} H \\ CH_3 \end{matrix}$ obtained by reducing the chloride is, however, optically inactive, and cannot be resolved into active components.

4. **Trimethyl-acetic acid,** *pivalic acid*, $(CH_3)_3C \cdot CO_2H$, can be prepared from tertiary butyl cyanide (*Butleroff*, 1873). It melts at 35°, boils at 164°, and has an odour like that of acetic acid.

Of the **hexylic acids,** eight are theoretically possible, and of these seven are already known. The most important among them is **normal caproic** acid, $CH_3 \cdot (CH_2)_4 \cdot CO_2H$ (*Chevreul*, 1822), which is found in nature, *e.g.* in cocoa-nut oil, Limburg cheese, and as a glyceride in the butter made from goats' milk, and is produced in the butyric fermentation of sugar, and by the oxidation of albuminous compounds and of the higher fatty acids, &c. Like valeric acid, it has a persistent odour of perspiration and rancid butter. B.-pt. 205°.

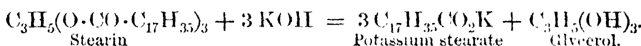
The higher acids found in nature are all of normal constitution, and contain an even number of carbon atoms. Goats' butter contains the acids C_6, C_8, and C_{10}, hence the names **caproic, caprilic,** and **capric** acids, and cocoa-nut oil—in addition to those three—the acid C_{12}. This last, **lauric acid,** is contained more especially in oil of laurels (*Laurus nobilis*); **myristic,** C_{14}, is present in oil of iris and nutmeg butter (from *Myristica moschata*); **arachidic,** C_{20}, in ground-nut oil (*Arachis hypogæa*); **behenic,** C_{22}, in the oil of ben (*Moringa oleifera*); **lignoceric,** C_{24}, in the oil from *Adenanthera pavonina*; **cerotic,** C_{26}, forms in the free state the chief constituent of bees'-wax, and as ceryl ester that of Chinese-wax. **Palmitic acid,** $C_{16}H_{32}O_2$, and **stearic acid,** $C_{18}H_{36}O_2$ (pp. 164 and 167), are very widely distributed, being nearly always accom-

panied by a third acid poorer in hydrogen, viz. **oleic acid**, $C_{18}H_{34}O_2$ (see Unsaturated Acids).

Most animal and vegetable fats and oils, *e.g.* tallow, suet, butter, palm, olive and seal oils, consist almost entirely of glycerides, viz. the glyceryl esters of palmitic, stearic, and oleic acids; these esters being termed, for the sake of brevity, **palmitin**, $C_3H_5(O\cdot CO\cdot C_{15}H_{31})_3$, **stearin**, $C_3H_5(O\cdot CO\cdot C_{17}H_{35})_3$, **olein**, $C_3H_5(O\cdot CO\cdot C_{17}H_{33})_3$. As palmitin and stearin are solid and olein liquid, the consistence of a fat or oil depends on the preponderance or otherwise of the solid esters. The constitution of the fats was elucidated by *Chevreul* in 1811. Rancidity consists of partial saponification in most cases and subsequent oxidation, whereby strongly smelling fatty acids are set free.

Most of the varieties of wax are, on the contrary, esters of monohydric alcohols; thus bees'-wax consists of the **melissic ester of palmitic acid**, $C_{30}H_{61}O\cdot CO\cdot C_{15}H_{31}$, together with free **cerotic acid**, Chinese wax (from *Croton sebiferum*, the tallow-tree) of the ester $C_{27}H_{55}O\cdot CO\cdot C_{26}H_{53}$, and spermaceti (Cetaceum, in the skull of *Physiter macrocephalus*) of the ester $C_{16}H_{33}O\cdot CO\cdot C_{15}H_{31}$.

From all these esters the acids are obtained in the form of potassium salts by saponification with alcoholic potash, thus:—



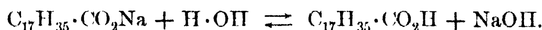
$$\underset{\text{Stearin}}{C_3H_5(O\cdot CO\cdot C_{17}H_{35})_3} + 3\,KOH = \underset{\text{Potassium stearate}}{3\,C_{17}H_{35}CO_2K} + \underset{\text{Glycerol.}}{C_3H_5(OH)_3}.$$

The separation of the acids is effected by fractional crystallization, fractional precipitation with magnesium acetate, or by fractional distillation either of the fats themselves or of their esters in a high vacuum. Oleic acid can be separated from palmitic and stearic by taking advantage of the solubility of its lead salt in ether or alcohol.

The stearine candles of commerce consist of a mixture of palmitic with excess of stearic acid, some paraffin wax being usually added to prevent them becoming crystalline. The manufacture of candles depends upon the saponification of the solid fats, especially of beef and mutton tallow, by means of water and lime, of concentrated sulphuric acid, of super-heated steam, or of Twitchell's reagent.

Soaps consist of the alkaline salts of palmitic, stearic, and oleic acids, hard soaps containing sodium salts, chiefly of the solid acids while soft soaps contain potassium salts, principally oleate. By the addition of common salt to a solution of a potassium soap, the latter is converted into a sodium soap, which is insoluble in

a solution of sodium chloride. This process is usually termed "*salting out*", and is analogous to the precipitation of sodium chloride by the addition of hydrogen chloride to its saturated solution. (Cf. *Walker*, "Phys. Chem.", Chap. XXII.) These alkali soaps dissolve to a clear solution in a little water, but with excess of water are hydrolyzed to a certain extent, yielding free alkali and free fatty acid or acid salt, analagous to potassium peracetate. The cleansing action of soap is usually attributed to the presence of the small amount of free alkali thus formed:



$$C_{17}H_{35} \cdot CO_2Na + H \cdot OH \rightleftarrows C_{17}H_{35} \cdot CO_2H + NaOH.$$

This hydrolysis is similar to that observed in the case of inorganic salts derived from a feeble acid and a strong base, and increases with increasing dilution. The production of free alkali (or free hydroxyl ions) can be readily understood by aid of the theory of ionization. The salt $R \cdot CO_2Na$, when dissolved in water, may be assumed to be ionized to a certain extent in the normal manner, thus giving rise to cations $\overset{+}{Na}$ and anions $R \cdot \overset{-}{CO_2}$. But water itself is ionized to a slight extent to $\overset{+}{H}$ and $\overset{-}{OH}$ ions, and we should thus have $\overset{+}{H}$ and $R \cdot \overset{-}{CO_2}$ ions in the same solution; the acid from which the sodium salt is derived is a feeble acid, and hence shows little tendency to ionize, and thus the $\overset{+}{H}$ and $R \cdot \overset{-}{CO_2}$ ions will unite to form non-ionized molecules $R \cdot CO_2H$. This implies removal of hydrions from the sphere of chemical action, and a certain number of water molecules will be ionized in order to supply fresh hydrions; these will again unite with the acid ions, and the two reactions will proceed until a state of equilibrium is established. In this state of equilibrium we shall have $R \cdot \overset{-}{CO_2}$, $\overset{+}{Na}$, $\overset{+}{H}$, $\overset{-}{OH}$ ions and $R \cdot CO_2H$ and H_2O molecules; but it is obvious that the $\overset{-}{OH}$ ions will be largely in excess of the $\overset{+}{H}$ ions, since a considerable number of these latter have been used up in forming non-ionized molecules of acid. The solution, as a whole, will thus possess more or less pronounced alkaline properties. (Cf. *Walker*, "Phys. Chem.", Chap. XXX.) The calcium, barium, and magnesium salts are insoluble in water, but partly crystallizable from alcohol. The precipitates produced by the action of hard water on soaps consist

largely of those insoluble salts. The lead salts (lead plaisters) are prepared by boiling fats with lead oxide and water.

Mixed glycerides occur in certain fats, *e.g.* $C_3H_5(O\cdot CO\cdot C_{15}H_{31})(O\cdot CO\cdot C_{17}H_{35})_2$ in lard (Abs., 1913, i, 441), butter (*ibid.*, 1040), beef fat, and in palm kernel oil. For general account of fats see *Armstrong* and *Allan*, J. Ind., 1924, 207 T.

For electrical conductivity of soap solutions, cf. *Banbury* and *Martin*, J. C. S. 1914, **105**, 417; *M'Bain* and *Martin*, *ibid.*, 957, and for detergent action, cf. *Pickering*, *ibid.*, 1917, **111**, 86.

The higher acids with an uneven number of carbon atoms, C_{11}, C_{13}, C_{15}, and C_{17}, are prepared synthetically from the acids containing 1 atom of carbon more, by transforming them into the ketones $C_{n-1}H_{2n-1}\cdot CO\cdot CH_3$ (p. 138), and oxidizing these, when acids $C_{n-2}H_{2n-3}\cdot COOH$ are obtained. (*Krafft.*)

On these reactions a method for proving that the higher fatty acids, *e.g.* palmitic and stearic, are normal in constitution has been based. (See Caution, p. 139.)

The acid $C_{15}H_{31}\cdot CO_2H$ is converted into the ketone $C_{15}H_{31}\cdot CO\cdot CH_3$; this on oxidation yields $C_{14}H_{29}\cdot CO_2H$ and acetic acid. The conversion into ketone and subsequent oxidation is repeated, and an acid, $C_{13}H_{27}\cdot CO_2H$, obtained. The processes are repeated until an acid, $CH_3\cdot(CH_2)_7\cdot CO_2H$, *n*-nonylic acid, is obtained. This can be shown to have a normal structure by synthetical methods, and hence all the higher acids must also have a normal structure, since if the acid $C_{13}H_{27}\cdot CO_2H$ had not a normal structure, but contained a side chain, *e.g.* $\begin{matrix}CH_3\\C_{11}H_{23}\end{matrix}\!\!>\!CH\cdot CO_2H$, on conversion into the ketone and subsequent oxidation it would not yield the acid, $C_{12}H_{25}\cdot CO_2H$, but a ketone, $CH_3\cdot CO\cdot C_{11}H_{23}$, or the oxidation products of this ketone.

Dissociation constant. — One of the most characteristic physical constants of the organic acids is what is termed the dissociation or affinity constant K, which is derived from the equation $k = \frac{a^2}{v(1-a)}$, where v = volume of solution in litres containing 1 gram mol. of the acid, a is the amount ionized, and $1-a$ the amount not ionized. This equation is based on the law of mass action. In the case of any feeble organic acid, *e.g.* acetic acid, where we have 1 gram molecule dissolved in v litres of solution, a state of equilibrium represented by the equation $CH_3\cdot COOH \rightleftharpoons CH_3\bar{\cdot}COO + \overset{+}{H}$ occurs.

Then if k_1 and k_2 represent the velocity constants of the direct and reverse reactions, we have, according to *Guldberg* and *Waage's* law, at the stage of equilibrium:—

$$k_1 \times \frac{1-a}{v} = k_2 \times \frac{a}{v} \times \frac{a}{v}, \text{ or } \frac{a_2}{v(1-a)} = \frac{k_1}{k_2} = k.$$

The extent of ionization in a solution containing 1 gram molecule in v litres is determined by electrical conductivity determinations. $a = \mu_v/\mu_x$, *i.e.* the degree of ionization at a dilution v is the ratio of the molecular conductivity at this dilution to the molecular conductivity at infinite dilution when all the acid molecules are ionized. (Cf. *Walker*, Chap. XXV.) For a weak acid, k remains constant, and affords a convenient measure of the strength of an organic acid. As a rule, the constant is usually taken as 100 times k, or K = 100 k.

Acid.	Formic.	Acetic.	Propionic.	*n*-Butyric.	*iso*-Butyric.
K.......	0·0214	0·00180	0·00134	0·0015	0·00144

Formic acid is obviously much the strongest of the fatty acids, but they are all comparatively weak acids compared with the strong mineral acids. Close comparison cannot be drawn between the two groups, as the equation $k = \frac{a^2}{(1-a)v}$ does not hold good for strong acids.

Palmitic Acid (*hexadecane. acid*), $CH_3 \cdot (CH_2)_{14} \cdot CO_2H$, is most conveniently prepared from palm-oil; also by fusing oleic acid or cetyl alcohol with potash.

Stearic acid, $CH_3 \cdot (CH_2)_{16} \cdot CO_2H$, is formed, among other methods, by reducing oleic acid, and is also obtained from the so-called shea-butter or from mutton suet.

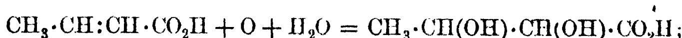
B. Unsaturated Acids, $C_nH_{2n-2}O_2$ or $C_mH_{2m-1} \cdot CO_2H$

	Melting pt.	Boiling-pt.
Acrylic acid, $C_3H_4O_2$	7°	140°
Crotonic acids, $C_4H_6O_2$.... 1 *a*	72°	182°
Crotonic acids, $C_4H_6O_2$.... 1 *b*	15°	172°
Crotonic acids, $C_4H_6O_2$.... 2	16°	160°
Angelic acid $C_5H_8O_2$	45°	185°
Tiglic acid $C_5H_8O_2$	65°	198°
Oleic acid, $C_{18}H_{34}O_2$	14°	...
Erucic acid, $C_{22}H_{42}O_2$..........	33°	...

These acids are known as the acids of the **oleic series.** In their physical properties they closely resemble the saturated acids, apart from differences in melting-point, which are appreciable. They have the chemical characteristics of monobasic acids; they yield salts, esters, amides, &c., in much the same manner as the saturated acids; but in addition they resemble the olefines in the readiness with which they yield additive compounds with hydrogen, halogens, halogen hydrides, or hydrogen cyanide, thus forming fatty acids or their substitution derivatives. Thus oleic acid, $C_{18}H_{34}O_2$, when treated with H_2 in presence of colloidal Pd, yields stearic acid, $C_{18}H_{36}O_2$, and with bromine, dibromo-stearic acid, $C_{18}H_{34}Br_2O_2$. In this way they characterize themselves as derivatives of the unsaturated hydrocarbons of the ethylene series, from which we may imagine them to be formed by the replacement of an atom of hydrogen by carboxyl. They may therefore be termed olefine-carboxylic acids.

Upon the addition of halogen hydride, the halogen does not always attach itself to that carbon atom to which the smaller number of hydrogen atoms is united.

The presence of the double bonds renders them much more sensitive to oxidizing agents than are the fatty acids. When a very dilute oxidizing agent is employed, *e.g.* 1 per cent permanganate, dihydroxy derivatives of fatty acids are obtained:



$$CH_3 \cdot CH:CH \cdot CO_2H + O + H_2O = CH_3 \cdot CH(OH) \cdot CH(OH) \cdot CO_2H;$$

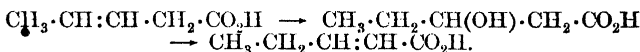
but if stronger oxidizing agents are employed, a rupture of the molecule occurs at the position where the double bond exists, and a mixture of acids is obtained:



$$CH_3 \cdot CH:CH \cdot CH_2 \cdot CO_2H \longrightarrow CH_3 \cdot CO_2H \text{ and } CO_2H \cdot CH_2 \cdot CO_2H.$$

This affords an excellent method for determining the position of the double bond in the molecule of the acid. Fusion with caustic alkalis also causes a breaking up of the molecules, and the formation of a mixture of fatty acids; but this reaction is of no use for determining the position of the double bond, as treatment with alkali tends to shift the double bond, if possible, nearer to the carboxylic group. *Fittig* (B. 1891, **24**, 82, &c.) has studied the action of dilute alkalis on a number of unsaturated acids, and always observed the same effect, *e.g.* the acid, $CH_3 \cdot CH_2 \cdot CH:CH \cdot CH_2 \cdot COOH$, passes into

$CH_3 \cdot CH_2 \cdot CH_2 \cdot CH:CH \cdot COOH$ (*2-hexene-1-acid*). Such changes, which are termed "molecular transformations", are explained by the assumption that atoms or radicals (in this case the elements of water) are added on to the original compound, and then eliminated in a different manner, *e.g.*:

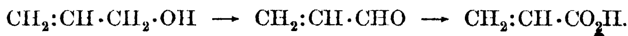

$$CH_3 \cdot CH:CH \cdot CH_2 \cdot CO_2H \rightarrow CH_3 \cdot CH_2 \cdot CH(OH) \cdot CH_2 \cdot CO_2H \rightarrow CH_3 \cdot CH_2 \cdot CH:CH \cdot CO_2H.$$

The presence of the double bond in the molecule has a considerable effect upon certain properties of the acid; for example, the dissociation constant and the rate of esterification by the catalytic method.

Fichter and *Pfister* have shown (Abs. 1904, i. 965) that the introduction of a double bond usually increases the strength of an acid, and that the effect is most marked when the double bond is in the β-γ-position, *e.g.* butyric acid, K = 0·00154; crotonic acid, K = 0·00204; and for vinyl acetic, K = 0·00383.

Sudborough (J. C. S. 1905, 1840; 1907, 1033; 1909, 315, 975) has shown that the introduction of the double bond in the α-position greatly retards esterification. The rates for hydrocinnamic, $C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CO_2H$, and for cinnamic acid, $C_6H_5 \cdot CH:CH \cdot CO_2H$, are as 40:1.

Modes of Formation.—1. By oxidizing the corresponding alcohols or aldehydes, *e.g.* acrylic acid from allyl alcohol or acrolein.


$$CH_2:CH \cdot CH_2 \cdot OH \rightarrow CH_2:CH \cdot CHO \rightarrow CH_2:CH \cdot CO_2H.$$

2. From the unsaturated alcohols or their iodides, by converting them into nitriles and hydrolysing these, *e.g.* crotonic acid from allyl iodide (intramolecular rearrangement, p. 170).


$$CH_2:CH \cdot CH_2I \rightarrow CH_3 \cdot CH:CH \cdot CN \rightarrow CH_3 \cdot CH:CH \cdot CO_2H.$$

Both these methods of formation are analogous to those of the fatty acids.

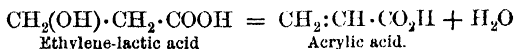
3. From the monohalogen substitution products of the saturated fatty acids, by warming with alcoholic potash, sometimes upon simply heating with water. This reaction is analogous to the formation of the olefines from alkyl haloids; it occurs in the case of those substituted acids which contain the halogen in the β-position to the carboxyl (see p. 173 *et seq.*).

4. From the halogen substitution products of the unsaturated acids by inverse substitution:



$$CH_3 \cdot CH:CCl \cdot CO_2H \longrightarrow CH_3 \cdot CH:CH \cdot CO_2H.$$

5. By the elimination of water from hydroxy fatty acids.



$$\underset{\text{Ethylene-lactic acid}}{CH_2(OH) \cdot CH_2 \cdot COOH} = \underset{\text{Acrylic acid.}}{CH_2:CH \cdot CO_2H} + H_2O$$

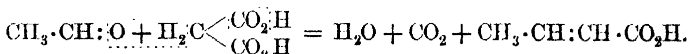
This reaction corresponds with the formation of the olefines from monohydric alcohols.

Constitution and Isomers.—The constitution of the unsaturated acids, $C_nH_{2n-2}O_2$, follows from their behaviour as monobasic acids and as unsaturated compounds, and the position of the double bond is ascertained by the process of oxidation. The number of isomeric acids, $C_mH_{2m-1} \cdot CO_2H$, is the same as the number of isomeric unsaturated alcohols, $C_mH_{2m-1} \cdot OH$.

Acrylic acid, *propene acid, ethylene-carboxylic acid,* $CH_2:CH \cdot CO_2H$ (*Redtenbacher*), is prepared by the oxidation of acrolein by oxide of silver, or by the distillation of β-iodopropionic acid with oxide of lead. (Cf. mode of formation 3.) It is very similar to propionic acid. Mixes with water and readily polymerizes. It is reduced to propionic acid when warmed with zinc and sulphuric acid, and is decomposed when fused with alkali into acetic and formic acids.

Acids, $C_4H_6O_2$. Four isomeric acids with this formula are known. 1. Ordinary or solid **crotonic acid** (*2-Buten-1-acid*), $CH_3 \cdot CH : CH \cdot CO_2H$, occurs along with isocrotonic acid in crude pyroligneous acid, and is prepared from allyl iodide by means of the cyanide, which, instead of having the anticipated formula, $CH_2 : CH \cdot CH_2 \cdot CN$, has the isomeric one, $CH_3 \cdot CH:CH \cdot CN$; this affords another example of molecular transformation.

It is also prepared by heating malonic acid with paraaldehyde and glacial acetic acid:



$$CH_3 \cdot CH:O + H_2C{<}{\begin{matrix}CO_2H\\CO_2H\end{matrix}} = H_2O + CO_2 + CH_3 \cdot CH:CH \cdot CO_2H.$$

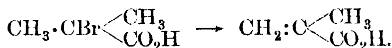
It crystallizes in large prisms, melts at 72°, boils at 189°, has an odour like that of butyric acid, and is fairly soluble in water. On reduction it yields *n*-butyric acid, and on careful oxidation, oxalic acid, hence the constitution.

2. Isocrotonic acid, $CH_3 \cdot CH:CH \cdot CO_2H$, obtained by the

action of sodium amalgam upon chloro-isocrotonic acid, melts at 15°, boils at 172°, and changes into ordinary crotonic acid at 180°. It is present in croton-oil. For preparation of the pure acid see *Morrell* and *Bellars*, J. C. S. 1904, 345.

Isocrotonic acid was formerly regarded as $CH_2:CH\cdot CH_2\cdot CO_2H$, but it shows almost the same chemical behaviour as crotonic acid, *e.g.* on reduction and oxidation, or on addition of hydrogen bromide, and is now regarded as having the same structural formula as, but being stereo-isomeric with, solid crotonic acid. (Cf. Fumaric and Maleic acids.)

3. **Meth-acrylic acid,** *2-methyl-2-propene-1-acid*, $CH_2:C<^{CH_3}_{CO_2H}$, is found in small quantity in Roman chamomile oil, and may be obtained by the withdrawal of HBr from bromo-isobutyric acid:



$$CH_3\cdot CBr<^{CH_3}_{CO_2H} \rightarrow CH_2:C<^{CH_3}_{CO_2H}.$$

It smells like decaying mushrooms, and melts at 15°.

4. **Vinyl-acetic acid,** $CH_2:CH\cdot CH_2\cdot CO_2H$, *1-Butene-4-acid*, may be obtained synthetically.

Angelic acid, $CH_3\cdot CH:C(CH_3)CO_2H$, is present in the angelica root, and, together with its stereo-isomer, **tiglic acid,** in Roman chamomile oil. (Cf. A. **250**; **259**, 24; **272**, 1; **273**, 127.) The relationship of these two acids is exactly the same as that of crotonic and isocrotonic acids.

Oleic acid, $C_{18}H_{34}O_2$ (*Chevreul*), is present as olein (glyceryl oleate) in the fatty oils especially, *e.g.* olive, almond, and train oils. It is a colourless oil, solidifies to white needles in the cold, melts at 14°, and cannot be volatilized without decomposition. It is tasteless and odourless, and has no action upon litmus, but quickly becomes yellow and acid by oxidation in the air, and also acquires a rancid odour. Its lead salt is soluble in ether, and by this means the acid may be separated from numerous other organic acids. It yields, on fusion with potash, the saturated acids, palmitic and acetic. Nitrous acid converts it into the stereo-isomeric crystalline **elaïdic acid,** melting at 45°. It contains a normal chain, since on reduction it yields stearic acid. When carefully oxidized, it yields **pelargonic acid,** $CH_3\cdot(CH_2)_7\cdot CO_2H$, and **azelaic acid,** $CO_2H\cdot(CH_2)_7\cdot CO_2H$, and hence the constitutional formula: $CH_3\cdot(CH_2)_7\cdot CH:CH\cdot(CH_2)_7\cdot CO_2H$. Isomers containing the olefine linking in a different position are known, *e.g.* Δ^2 acid.

Erucic acid, $C_{22}H_{42}O_2$, occurs in rape-seed oil, melts at 33°, and on treatment with nitrous acid yields the stereo-isomeric **brassidic acid,** melting at 60°. The constitution is probably, $CH_3[CH_2]_7\cdot CH:CH[CH_2]_{11}\cdot CO_2H$. For the stereo-chemistry of the unsaturated acids, see Fumaric and Maleic acids.

C. Propiolic Acid Series, $C_nH_{2n-4}O_2$

The acids of this series again contain two atoms of hydrogen less than those of the former, and are to be regarded as carboxylic acids of the acetylene hydrocarbons, *e.g.* propiolic acid, $CH\vdots C\cdot CO_2H$, as acetylene-carboxylic acid. They can accordingly be prepared by the addition of CO_2 to the sodium derivatives of the acetylenes (analogously to mode of formation 4 of the saturated acids, p. 140).

They closely resemble the unsaturated acids which have been already described, but differ from them by the fact that each molecule of such an acid can combine with either 2 or 4 atoms of hydrogen, chlorine, bromine, &c., and can yield explosive compounds with ammoniacal silver and copper solutions. There are, however, acids of the formula $C_nH_{2n-4}O_2$ which do not possess this last peculiarity, viz., those which are derived, not from the homologues of acetylene proper, but from their isomers, and which therefore contain two double bonds instead of a triple one. (Compare Acetylene Hydrocarbons, p. 54.)

The most important member of the series is **propiolic** or **propargylic acid,** *propine acid*, $CH\vdots C\cdot CO_2H$, which corresponds with propargyl alcohol, and is prepared by warming an aqueous solution of the acid potassium salt of acetylene-dicarboxylic acid, the latter being itself obtained from dibromosuccinic acid. (See p. 249, also B. **18,** 677.) In its physical properties it resembles propionic acid, forms silky crystals below 6°, and boils at 144°. It is readily soluble in water and alcohol, and becomes brown in the air. It gives, even in dilute solution, the characteristic explosive silver precipitate.

Tetrolic acid, $CH_3\cdot C\vdots C\cdot CO_2H$, is obtained from β-chlorocrotonic acid and aqueous potash, and melts at 76°.

Sorbic acid, $CH_3\cdot CH:CH\cdot CH:CH\cdot CO_2H$, is contained in the juice of the unripe sorb apple (*Sorbus Aucuparia*), and has relatively high melting- and boiling-points.

Highly unsaturated normal acids, *e.g.* **linolic,** $C_{18}H_{32}O_2$, $\Delta^{9:12}$ diolefine acid, and **linolenic,** $C_{18}H_{30}O_2$, $\Delta^{9:11:13}$ triolefine acid, occur as glycerides in many marine and some vegetable oils.

D. Halogen Substitution Products of the Monobasic Acids

The saturated monobasic acids yield halogen substitution products, *e.g.*:

Name.	Formula	Melting-pt.	Boiling-pt.	K.
Acetic acid	$CH_3 \cdot CO_2H$	17°	118°	0·00180
Chlor-acetic acid	$CH_2Cl \cdot CO_2H$	62°	186°	0·155
Dichlor-acetic acid	$CHCl_2 \cdot CO_2H$	liq.	191°	5·14
Trichlor-acetic acid	$CCl_3 \cdot CO_2H$	52°	195°	121·0
Brom-acetic acid	$CH_2Br \cdot CO_2H$	50°	208°	0·138
Dibrom-acetic acid	$CHBr_2 \cdot CO_2H$	48°	232°	...
Tribrom-acetic acid	$CBr_3 \cdot CO_2H$	135°	dec.	...
Iodo-acetic acid	$CH_2I \cdot CO_2H$	82°	dec.	0·075
Cyano-acetic acid	$CN \cdot CH_2 \cdot CO_2H$	65°	dec.	0·370
Propionic acid	$CH_3 \cdot CH_2 \cdot CO_2H$	− 23°	140·7°	0·00134
α-Chloro-propionic acid	$CH_3 \cdot CHCl \cdot CO_2H$	oil	186°	...
β-Chloro-propionic acid	$CH_2Cl \cdot CH_2 \cdot CO_2H$	41·5° (?)	204°	...
α-Bromo-propionic acid	$CH_3 \cdot CHBr \cdot CO_2H$	24·5°	203·5°	...
β-Bromo-propionic acid	$CH_2Br \cdot CH_2 \cdot CO_2H$	62·5°	...	...
α-Iodo-propionic acid	$CH_3 \cdot CHI \cdot CO_2H$	oil	...	...
β-Iodo-propionic acid	$CH_2I \cdot CH_2 \cdot CO_2H$	82°	...	0·009
α:β-Dibromo-propionic acid	$CH_2Br \cdot CHBr \cdot CO_2H$	64°	...	...
α:α-Dibromo-propionic acid	$CH_3 \cdot CBr_2 \cdot CO_2H$	61°	...	3·3
β:β-Dibromo-propionic acid	$CHBr_2 \cdot CH_2 \cdot CO_2H$	71°	...	...

The unsaturated acids also yield similar substitution products, *e.g.* $CH_2:CCl \cdot CO_2H$, α-chlor-acrylic acid; $CHBr:CH \cdot CO_2H$, β-brom-acrylic acid; $CH_3 \cdot CH:CCl \cdot CO_2H$, α-chlor-crotonic acid; $CI:C \cdot CO_2H$, iodo-propiolic acid, &c.

All these halogen derivatives have the properties of monobasic acids; in many respects they resemble the parent substances, but as a rule are much stronger acids. This is extremely well shown in a comparison of the dissociation constants K. (See table.)

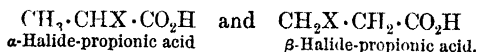
Since their acid nature remains unaltered, they still contain the carboxyl group; the halogen has therefore replaced the hydrogen of the hydrocarbon radical. They may also be looked upon as halide substitution products of the hydrocarbons, in which 1 atom of hydrogen is replaced by carboxyl:



CH_3Cl (chloro-methane) $CH_2Cl \cdot CO_2H$ (chlor-acetic acid).

The modes of formation and properties of these substituted acids also coincide with this view. Thus, while they show a behaviour perfectly analogous to that of the non-substituted acids, forming salts, esters, chlorides, anhydrides, and amides their halogen atoms are as readily exchangeable for OH, CN, or SO_3H, as are those of the substitution products of the hydrocarbons. (See p. 64.)

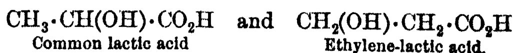
Isomers and Constitution.—While in each case only one mono-, di-, &c., halide acetic acid exists, two isomeric monohaloid propionic acids are known. This is readily explicable from the fact that in propionic acid, $\overset{\beta}{CH_3} \cdot \overset{\alpha}{CH_2} \cdot CO_2H$, the two α-hydrogen atoms are differently situated from the three β- ones, the former being attached to the carbon atom nearer to the carboxyl, and the latter to that one farther from it. According to theory, therefore, with which the observed facts agree, the following two isomers are possible:—



$CH_3 \cdot CHX \cdot CO_2H$ and $CH_2X \cdot CH_2 \cdot CO_2H$

α-Halide-propionic acid β-Halide-propionic acid.

These acids yield two isomeric lactic acids by exchange of their halogen for hydroxyl, thus:—



$CH_3 \cdot CH(OH) \cdot CO_2H$ and $CH_2(OH) \cdot CH_2 \cdot CO_2H$

Common lactic acid Ethylene-lactic acid.

The constitution of both of these lactic acids follows from their other modes of formation (see p. 215, *et seq.*). The

positions of the halogens in the α- and β- substituted propionic acids are thus also fixed.

Those substituted acids which contain the halogen attached to the α-carbon atom, *i.e.* to the same carbon atom to which the carboxyl group is united, are termed α-acids, and the others β, γ, &c., acids, the successive carbon atoms in their order from the carboxyl group being designated as α, β, γ, &c.

We thus distinguish, for instance, between α-, β-, and γ-chloro-butyric acids, αα-, αβ-, and ββ- dibromo-propionic acids, &c.

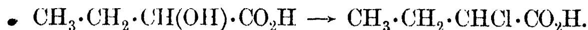
Two stereo-isomeric forms of the α- or β- mono-chloro- and -bromo-crotonic acids are known (A. **248**, 281), being derived from crotonic and isocrotonic acids respectively.

Formation.—(*a*) Of the saturated substituted acids.

1. Chlorine and bromine can substitute directly, the halogen taking up the α-position to the carboxyl.

The reaction is often carried out in sunlight and in the presence of a halogen carrier. One of the commonest methods is to transform the acid into the acid bromide by the aid of phosphorus and bromine, and then to brominate. The product obtained, *e.g.* $CH_3\cdot CHBr\cdot COBr$, on treatment with water yields the α-bromo acid, $CH_3\cdot CHBr\cdot CO_2H$. This is generally known as the *Hell-Volhard-Želinsky* method. Trimethyl acetic acid, $CMe_3\cdot CO_2H$, which contains no α-hydrogen atom, cannot be brominated in this manner (B. 1890, **23**, 1594). (Cf. Chap. XLVII, G.)

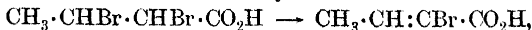
2. From hydroxy acids of the glycollic series by the action of PCl_5, HBr, &c., *e.g.*:



$$CH_3\cdot CH_2\cdot CH(OH)\cdot CO_2H \longrightarrow CH_3\cdot CH_2\cdot CHCl\cdot CO_2H.$$

3. By the addition of halogen or halogen hydride to the unsaturated acids.

(*b*) Of the unsaturated substituted acids. These are often prepared by the elimination of HCl, HBr, or HI from poly-halogen derivatives of the fatty acids:



$$CH_3\cdot CHBr\cdot CHBr\cdot CO_2H \longrightarrow CH_3\cdot CH{:}CBr\cdot CO_2H,$$

or by the addition of hydrogen halide to propiolic acids.

Behaviour.—1. For the replacement of chlorine, bromine, and iodine by hydroxyl, see p. 214. This exchange takes place with more difficulty in the α-monochloro-substituted acids than in the corresponding bromine and iodine compounds, but more easily than in the case of the alkyl chlorides, and it is effected by means of moist silver oxide,

or frequently by prolonged boiling with water alone (A. **200**, 75). In this way monochlor-acetic yields glycollic acid:



$$CH_2Cl \cdot CO_2H + H_2O = OH \cdot CH_2 \cdot CO_2H + HCl.$$

β-halogen acids, on the other hand, lose halogen hydride when boiled with water, and yield unsaturated acids, together with CO_2 and olefines $C_{n-1}H_{2n-2}$. γ-halogen acids break up under these conditions (even with cold soda solution) into HCl, &c., and a lactone, *i.e.* an anhydride of a γ-hydroxy-acid (see p. 225; cf. *Fittig*, A. **208**, 116).

2. When boiled with an alcoholic solution of potassium cyanide, cyano-fatty acids* are produced.



$$CH_2Cl \cdot CO_2K + KCN = CN \cdot CH_2 \cdot CO_2K + KCl.$$

These compounds are on the one hand monobasic acids, and on the other nitriles, and they consequently yield dibasic acids when hydrolysed. In the above case malonic acid, $CO_2H \cdot CH_2 \cdot CO_2H$, is formed.

3. They form sulphonic acids with sodium sulphite, *e.g.*:



$$CH_2Cl \cdot CO_2Na + Na \cdot SO_3Na = NaSO_3 \cdot CH_2 \cdot CO_2Na + NaCl.$$

These latter are compounds and are dibasic acids as they contain both CO_2H and SO_3H groups. Their sulpho-group can, however, be replaced by OH on boiling with alkalis.

4. With $AgNO_2$, under favourable conditions, nitro-derivatives of the fatty acids are formed, and these yield amino-acids on reduction *e.g.* $NH_2 \cdot CH_2 \cdot CO_2H$. (B. 1910, **43**, 3239.)

Chloroformic acid, $Cl \cdot CO_2H$, has so far not been prepared, although derivatives of it are known. (Cf. Chloro-carbonic acid.)

The chlorinated acetic acids are formed by the direct substitution of acetic acid, or better, of acetyl chloride, chlorinated acetyl chlorides ensuing in the latter case as intermediate products.

Monochlor-acetic acid (*Chloro-ethane acid*), $CH_2Cl \cdot CO_2H$, is prepared by chlorinating acetic acid, preferably in the presence of acetic anhydride, sulphur, or phosphorus. It forms rhombic prisms or tables and corrodes the epidermis. **Dichlor-acetic acid**, $CHCl_2 \cdot CO_2H$, is more conveniently obtained by warming chloral hydrate with potassium cyanide (B. **10**, 2120), and **trichlor-acetic acid**, $CCl_3 \cdot CO_2H$, by

* These can also be obtained by the addition of HCN to an olefine acid or ester (J. C. S., 1922, 1699).

oxidizing chloral hydrate with nitric acid. The former decomposes with boiling alkali to oxalic and acetic acids, and the latter to chloroform and carbon dioxide. Inverse substitution reconverts tri-, di-, and monochlor-acetic acids into acetic acid (*Melsens*, 1842).

Sulpho-acetic acid, $SO_3H \cdot CH_2 \cdot CO_2H$, forms deliquescent prisms containing $1\frac{1}{2}$ mols. H_2O of crystallization. Its salts crystallize well. **Cyano-acetic acid**, $CN \cdot CH_2 \cdot CO_2H$, is a crystalline substance melting at 65°–66° and readily soluble in water; it decomposes into aceto-nitrile, $CH_3 \cdot CN$, and CO_2 when heated, and yields malonic acid on hydrolysis.

α-Chloropropionic acid, $CH_3 \cdot CHCl \cdot CO_2H$, is obtained by the action of PCl_5 upon lactic acid, and decomposition of the lactyl chloride, $CH_3 \cdot CHCl \cdot COCl$, by water. The β-chloro- and bromo-acids are obtained from trimethyleneglycol (p. 199). **β-iodopropionic acid**, $CH_2I \cdot CH_2 \cdot CO_2H$, is prepared by the action of PI_3 on glyceric acid, $CH_2(OH) \cdot CH(OH) \cdot CO_2H$ (exchange of 2 OH for 2 I and of I for H; also by acting on acrylic acid with hydriodic acid. It forms colourless six-sided tables of a peculiar odour; m.-pt. 82°. The two **cyanopropionic acids**, $C_2H_4(CN) \cdot CO_2H$, give the two succinic acids when hydrolysed.

Chloro- and **Bromo-crotonic acids**, **β-Chloro-crotonic** acid (*2-Chloro-2-Butene acid*) (m.-pt. 94°) and the stereo-isomeric **β-Isochloro-crotonic acid** (m.-pt. 59·5°) are formed by the action of PCl_5 on ethyl acetoacetate, and treatment of the product with water. The β-chlor-iso-acid volatilizes with steam, but the β-chloro-acid does not.

VII. ACID DERIVATIVES

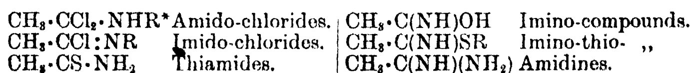
A general idea of the kind of derivatives to which acids give rise is obtained by comparing these derivatives with corresponding derivatives of the saturated monohydric alcohols, *e.g.* those of acetic acid with those derived from ethyl alcohol:

$CH_3 \cdot CH_2 \cdot OH$	Alcohol.	$CH_3 \cdot CO \cdot OH$	Acetic acid.
$CH_3 \cdot CH_2 \cdot ONa$	Sodium ethylate.	$CH_3 \cdot CO \cdot ONa$	Sodium acetate.
$\begin{matrix} CH_3 \cdot CH_2 \\ CH_3 \cdot CH_2 \end{matrix} > O$	Ethyl ether.	$\begin{matrix} CH_3 \cdot CO \\ CH_3 \cdot CH_2 \end{matrix} > O$	Ethyl acetate.
		$(CH_3 \cdot CO)_2O$	Acetic anhydride.
$CH_3 \cdot CH_2 \cdot Cl$	Ethyl chloride.	$CH_3 \cdot CO \cdot Cl$	Acetyl chloride.
$CH_3 \cdot CH_2 \cdot SH$	Mercaptan.	$CH_3 \cdot CO \cdot SH$	Thiacetic acid.
$CH_3 \cdot CH_2 \cdot NH_2$	Ethylamine.	$CH_3 \cdot CO \cdot NH_2$	Acetamide.

It is seen that as regards formulæ there is a close resemblance, the acetyl group taking the place of the ethyl group. Stated generally, the acid derivatives contain acyl radicals in place of the alkyl groups contained in the corresponding derivatives of alcohols.

These derivatives are obtained by methods many of which are perfectly analogous to the modes of formation of the corresponding alkyl derivatives, but they differ characteristically from these by being less stable towards hydrolysing agents.

A number of other derivatives, viz. amido- and imido-chlorides, thiamides, imido-thio-compounds, and amidines, are peculiar to the acids:



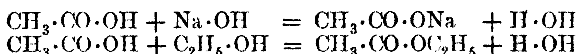
$CH_3 \cdot CCl_2 \cdot NHR$*	Amido-chlorides.	$CH_3 \cdot C(NH)OH$	Imino-compounds.
$CH_3 \cdot CCl{:}NR$	Imido-chlorides.	$CH_3 \cdot C(NH)SR$	Imino-thio- ,,
$CH_3 \cdot CS \cdot NH_2$	Thiamides.	$CH_3 \cdot C(NH)(NH_2)$	Amidines.

These compounds are also characterized by being readily hydrolysed.

A. Esters of the Fatty Acids

We have already seen that mineral acids readily give rise to esters by the replacement of their acidic hydrogen radicals by alkyl groups, *e.g.* $SO_2(OH)_2 \rightarrow SO_2(OEt)_2$. In exactly the same manner the typical hydrogen of the fatty acids can be replaced by alkyl groups, and we get esters derived from the fatty acids, *e.g.* ethyl acetate, $CH_3 \cdot CO_2Et$. Since these esters correspond with the metallic salts, they are sometimes termed alkyl salts. (Cf. $CH_3 \cdot CO_2K$ and $CH_3 \cdot CO_2Et$.)

Methods of Formation.—1. By direct **esterification**, *i.e.* by direct action of the acid on the alcohol:



$$CH_3 \cdot CO \cdot OH + Na \cdot OH = CH_3 \cdot CO \cdot ONa + H \cdot OH$$
$$CH_3 \cdot CO \cdot OH + C_2H_5 \cdot OH = CH_3 \cdot CO \cdot OC_2H_5 + H \cdot OH$$

Although the equation representing the reaction is analogous to that representing the neutralization of acetic acid by an alkali, the process of esterification differs from that of neutralization in two respects.

(1) The reaction proceeds but slowly; thus, in the esterification of acetic acid by ethyl alcohol the limit of the reaction at the boiling-point is not reached until after the lapse of

* R signifies an alkyl radical either alphyl or aryl.

several hours, and even then only two-thirds of the acid have been transformed into ester.

(2) The reaction is a reversible or balanced one, and hence is never complete. The water which is formed during the process of esterification tends to hydrolyse the ester back into acid and alcohol:



$$CH_3\cdot CO\cdot OH + C_2H_5\cdot OH \rightleftarrows CH_3\cdot CO\cdot OC_2H_5 + H\cdot OH.$$

Thus, when equivalent quantities of acetic acid and ethyl alcohol are employed, only some 66 per cent of the acid becomes transformed into ester. It can readily be shown, by aid of *Guldberg-Waage's* law of mass action, that by employing an excess of alcohol a larger proportion of acid will be converted into ester. Thus, in the above equation, if the original concentrations of the four substances expressed in gram molecules be denoted by a, b, o and o, and the velocity constants of the direct and reverse reactions by k_1 and k_2 respectively, then after time t equilibrium will be established; and if we assume x gram molecules of acid have been esterified, then the concentrations of the four substances will be $a - x$, $b - x$, x and x. The rate of the direct reaction can be denoted by $k_1 (a - x)(b - x)$, and that of the reverse by $k_2 x^2$ (*Guldberg and Waage*). When equilibrium is established, the two reactions will proceed at the same rate, and

$$k_1 (a-x)(b-x) = k_2 x^2,$$

$$\text{or } \frac{(a-x)(b-x)}{x^2} = \text{constant for a given temperature.}$$

In the case of acetic acid and ethyl alcohol, using gram molecular proportions, *i.e.* $a = b = 1$, we find that equilibrium is established when some two-thirds of acid are esterified. Thus

$$\frac{(1-\frac{2}{3})(1-\frac{2}{3})}{(\frac{2}{3})^2} = \text{constant,}$$

and the constant becomes equal to $\frac{1}{4}$.

Then, supposing we alter the proportions of acid and alcohol, using 2 gram molecules of alcohol to 1 of acid, we have—

$$\frac{(1-x)(2-x)}{x^2} = \frac{1}{4}.$$

$$x = \cdot 85 \text{ (approx.),}$$

and thus 85 per cent of the acid will have been esterified in place of the 66 per cent when only 1 gram. mol. of alcohol was used. The reversible nature of the reaction is of especial importance in the preparation of ethyl acetate, and in this case the difficulty is overcome by the addition of a moderate amount of concentrated sulphuric acid, which is ordinarily supposed to react with the water, and thus prevent its hydrolysing the ester. (Compare also *Wade*, J. C. S. 1905, 1656.)

It is worthy of note that the limit of esterification does not vary to any large extent with the temperature. Thus, in the case mentioned above, the limit at 10° is 65·2 per cent, and at 220° it is only 66·5 per cent.

With most of the higher esters, and more especially the esters in the aromatic series, the limit of esterification is much higher, as the esters are not so readily hydrolysable. In these cases, however, the rates at which the esters are formed are extremely slow, and a catalytic agent is therefore introduced. The two common catalytic agents employed are: (1) A small amount of dry hydrogen chloride. At one time it was customary to saturate the boiling alcoholic solution of the acid with hydrogen chloride, but the researches of *E. Fischer* and *Speier* (B. 1895, **28**, 3201, 3252) have shown that the addition of 3 per cent of dry hydrogen chloride to the alcoholic solution is quite sufficient. (2) A small amount of concentrated sulphuric acid, which acts in much the same manner as the hydrogen chloride. The use of these reagents is not to raise the limit of esterification, but to accelerate the production. In most cases, using the catalytic method at the boiling-point of the alcohol, the reaction is complete after three hours, and a 90–95 per cent yield of ester can be obtained by pouring into water.

A number of researches have been made as to the influence of the constitution of the acid and of the alcohol on the rate of esterification, *i.e.* the amount of ester formed in unit time. *Menschutkin*, who employed the direct esterification method without a catalytic agent, *i.e.* the so-called auto-catalytic method, found that primary acids, *i.e.* $R \cdot CH_2 \cdot CO_2H$, were esterified most quickly; secondary acids, $RR'CH \cdot CO_2H$, were intermediate; and tertiary acids, $RR'R''C \cdot CO_2H$, least readily when the same alcohol was employed. Other researches tend to show that strong acids react with alcohol more readily than feeble acids in the absence of a catalyst.

The velocity of esterification has also been determined for

a number of acids employing the catalytic method (HCl). From the equation we should expect the reaction to be a bimolecular reaction, or a reaction of the second order; by altering the conditions, namely, by taking a large excess of alcohol as compared with the acid, the concentration of the alcohol may be regarded as constant, and the reaction then becomes unimolecular (*H. Goldschmidt*) and may be studied by the aid of the equation for unimolecular reactions, $k = \frac{1}{t} \log. \frac{a}{a - x}$; where k = the velocity constant, t = time, a = concentration of the acid at the beginning of the experiment expressed in c.c. of standard alkali, and $a - x$ = concentration of the acid after the lapse of time t. The value of k diminishes with the time due to the inhibiting action of traces of water. Using this method, it is found that the introduction of any substituent (CH_3, Cl, Br, I, C_6H_5, &c.) into the acetic acid molecule lowers the velocity of esterification, the introduction of two such radicals, *e.g.* $CHBr_2 \cdot CO_2H$, lowers the constant still further, and when all three hydrogens are replaced by substituents, *e.g.* $C(CH_3)_3 \cdot CO_2H$, the acid is esterified very slowly indeed as compared with acetic acid.

These examples afford an extremely good instance of what is now generally termed **steric retardation**, or the retardation of a chemical reaction by the spatial relationships of radicals introduced into a molecule.

The common theory of the process of esterification is that there is first direct union between a molecule of the acid and of the alcohol.



yielding a dihydroxylic compound, which immediately eliminates water, yielding the ester $R \cdot C \lessgtr^{OR'}_{O}$. The introduction of radicals into the CH_3 group of the acetic acid molecule by filling up the space renders the formation of such additive compounds much more difficult, and hence the retardation of esterification (*Wegscheider*).

The influence of the hydrogen chloride is purely catalytic; it remains unchanged at the end of the reaction. Its catalysing effect is partly due to the hydrions it generates, as strong acids (HCl, HBr) are much better catalysing agents than

weaker acids (picric acid), but also to the undissociated molecules. (Cf. *Goldschmidt*, B. 1895, **28**, 3218; Z. elec. 1911, **17**, 684; *Snethlage*, Zeit. phys. 1915, **90**, 142.

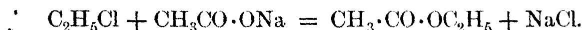
Ultra-violet light accelerates the reaction between organic acids and alcohols (B. 1914, **47**, 1803).

2. By the action of an acid chloride upon an alcohol or its sodium compound (cf. p. 185):



$$CH_3\cdot CO\cdot Cl + C_2H_5\cdot OH = CH_3\cdot CO\cdot O\cdot C_2H_5 + HCl.$$

3. By the action of alkyl halides upon salts of the acid:



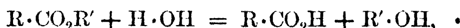
$$C_2H_5Cl + CH_3CO\cdot ONa = CH_3\cdot CO\cdot OC_2H_5 + NaCl.$$

As a rule, an alkyl iodide and the silver salt of the acid are employed. The ester can then be separated from the solid silver iodide and distilled. Occasionally the potassium salt and methyl sulphate are used. Reactions 2 and 3 are of very general application, and are largely made use of when an ester cannot readily be obtained by the catalytic method of esterification.

Properties.—The esters are mostly neutral liquids which volatilize without decomposition; only those which contain a small number of carbon atoms in the molecule are soluble in water, *e.g.* ethyl acetate (1:14).

1. **Hydrolysis.**—They are all hydrolysed (saponified), *i.e.* resolved back into alcohol and acid, when heated, or better, superheated, with water, or when boiled with aqueous solutions of strong alkalis or mineral acids; with the simpler esters this hydrolysis is complete when the ester is allowed to remain for some time in contact with water or dilute alkali.

The hydrolysis of an ester under the influence of water or of mineral acids may be represented by the equation:



$$R\cdot CO_2R' + H\cdot OH = R\cdot CO_2H + R'\cdot OH,$$

and may be studied by the aid of the general equation for a uni-molecular reaction, $k = \frac{1}{t}\log.\frac{a}{a-x}$, since the concentration of the water, if a large excess is used, may be regarded as constant.

The action of the mineral acid is purely catalytic. The same result might ultimately be obtained by using water alone, but is considerably accelerated by using a small amount of a strong mineral acid (HCl, H_2SO_4). Weak acids also accelerate the hydrolysis of the ester, but to a less extent. It

has been found, using the same ester and equivalent quantities of different acids, that the rate of hydrolysis is directly proportional to the strength of the acid. In other words, the catalysing influence of different acids is due to the hydrions.

The hydrolysis of an ester by alkalis is represented by the equation: $R \cdot CO \cdot OR' + NaOH = R \cdot CO \cdot ONa + R' \cdot OH$, and as it is analogous to the preparation of soaps by the action of alkalis on fats (p. 164), is commonly termed Saponification. This is a bimolecular reaction, and if equivalent quantities of ester and alkali are employed in solution, can be studied by aid of the equation $k = \frac{1}{t} \cdot \frac{x}{a(a-x)}$, where t = time, a = initial concentration of alkali and of ester, $a - x$ = concentration of these after time t. The concentrations can readily be determined by direct titration with standard acid, and the number of cubic centimetres of acid introduced directly into the equation.

It has been found that when different alkalis are employed, their hydrolysing effect is proportional to their strengths, *i.e.* is due to the free hydroxyl ions. Different esters are hydrolysed at very different rates by the same alkali; the rate appears to depend on the complexity of the molecule, *i.e* the number of substituents present, and also on the nature of these substituents, viz. whether they are of a positive or negative nature. It has been found that $CCl_3 \cdot CO_2C_2H_5$ is hydrolysed by alcoholic potash much more readily than ethyl acetate itself, owing to the negative nature of the chlorine substituents. (Compare A. **228**, 257; **232**, 103; J. C. S. 1899, 482.)

In all cases it has been found that, comparing solutions of equal strength, *e.g.* N/10, a strong alkali is a much better hydrolysing agent than a strong acid.

2. A characteristic reaction of methyl and ethyl esters is that they exchange OMe (**methoxy**) or OEt (**ethoxy**) groups for NH_2 on treatment with strong ammonia, thus yielding acid amides, *e.g.* $CH_3 \cdot CO \cdot NH_2$.

3. Phosphorus pentachloride decomposes most esters, yielding an alkyl chloride and an acyl chloride, the O of the $\cdot OEt$ group being replaced by two chlorine atoms

4. Ethyl esters are readily transformed into methyl esters, $R \cdot CO_2Et \rightarrow R \cdot CO_2Me$, by warming with methyl alcohol and a catalyst (CH_3ONa, HCl). The reaction is reversible, and is termed **alcoholysis.**

5. Sodium methoxide combines with the esters to form un-

stable additive compounds, $R \cdot C \begin{cases} ONa \\ OCH_3 \\ OR' \end{cases}$, which are derivatives of "ortho-acids". (See p. 148; also B. **20**, 646.)

The odour and taste of many of the esters is so agreeable that they are manufactured upon a large scale, and employed as fruit essences.

Ethyl formate, $H \cdot CO \cdot OC_2H_5$, b.-pt. 55°, is employed in the manufacture of artificial rum or arrak. **Ethyl acetate**, *acetic ether*, $CH_3 \cdot CO \cdot OC_2H_5$, b.-pt. 75°, is used internally as a medicine. **Amyl acetate**, $CH_3 \cdot CO \cdot OC_5H_{11}$, b.-pt. 148°. The alcoholic solution of this forms the essence of pears. **Ethyl butyrate**, $CH_3(CH_2)_2CO \cdot OC_2H_5$, is the essence of pine-apples. **Iso-amyl iso-valerate**, $C_4H_9 \cdot CO \cdot O \cdot OC_5H_{11}$, b.-pt. 196°, finds application as apple oil or apple ether. **Cetyl palmitate**, $C_{15}H_{31} \cdot CO \cdot OC_{16}H_{33}$, **ceryl cerotate**, $C_{25}H_{51} \cdot CO \cdot OC_{26}H_{53}$, and **melissic palmitate**, $C_{15}H_{31} \cdot CO \cdot O \cdot C_{30}H_{61}$, are constituents of waxes. (See Wax Varieties, p. 164.)

Ethyl acetate, which is used as a solvent and also for the preparation of ethyl aceto-acetate (Chap. IX, G.), is usually prepared from alcohol, acetic acid, and an excess of sulphuric acid. A recent method consists in passing aldehyde (prepared from acetylene) into a solution of aluminium ethoxide, $Al(OEt)_3$, in a high-boiling solvent. The yield is 85 per cent of the theoretical and the consumption of aluminium ethoxide is only 3–5 per cent (C. Z., 1918, ii, 693).

Although the reaction between alcohol and acetic acid is a balanced one and the water formed tends to decompose the ester, *Bodraux* (C. R., 1913, **156**, 1079; 1914, **157**, 938) has shown that a 92-per-cent yield of ethyl acetate is formed when a mixture of acetic acid and alcohol is boiled with a 10-per-cent aqueous solution of sulphuric acid, and the ester removed by distillation as fast as it is formed. Equally good results can be obtained with esters derived from other fatty acids and primary alcohols, provided the esters boil below 100°.

Esters of the higher acids when distilled under atmospheric pressure decompose into an olefine and a fatty acid. (See p. 49.)

n-Butyl acetate and *iso*-amyl acetate are manufactured for solvents for nitro cellulose paints and varnishes.

Isomers.—All esters containing the same number of C atoms in the molecule, and derived from the monohydric saturated alcohols and the fatty acids, are isomeric. Thus methyl butyrate is isomeric not only with ethyl propionate but also with

propyl acetate and with butyl formate. Further, all esters are isomeric with the monobasic acids which contain an equal number of carbon atoms, *e.g.* the esters just mentioned are isomeric with the valeric acids. (See Metamerism, p. 90.)

Further cases of isomerism occur when the alcohol on the one hand, or the acid on the other, is unsaturated, *e.g.* allyl propionate and propyl acrylate.

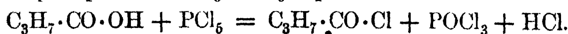
B. Acid Chlorides, Bromides, &c.

Acid chlorides are the compounds derived from the acids by the replacement of the hydroxyl group by chlorine:



$$R{\cdot}CO{\cdot}OH \longrightarrow R{\cdot}CO{\cdot}Cl.$$

1. They are usually prepared by the action of the chlorides of phosphorus, PCl_3, PCl_5, upon the acids.



$$C_3H_7{\cdot}CO{\cdot}OH + PCl_5 = C_3H_7{\cdot}CO{\cdot}Cl + POCl_3 + HCl.$$

The acid chloride is separated from the $POCl_3$ formed at the same time by fractional distillation. In the case of acetic acid PCl_3 is conveniently used:

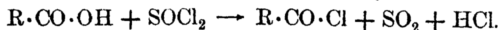


$$3\,CH_3{\cdot}CO{\cdot}OH + PCl_3 = 3\,CH_3{\cdot}CO{\cdot}Cl + PO_3H_3.$$

A recent process is the action of PCl_3 on a mixture of acid and acid anhydride. No HCl is evolved, and an 85 per cent yield of acid chloride is obtained. E.P. 26140 of 15, iii., 1926.

Phosphorus oxychloride, $POCl_3$, reacts with the alkali salts of the acids; the products are the acid chloride, and an alkali chloride and metaphosphate. When an alkali salt is used, an acid anhydride is formed in the absence of excess of the phosphorus halide (p. 187).

Thionyl chloride is now frequently used in place of chlorides of phosphorus as the acid chloride is readily isolated:



$$R{\cdot}CO{\cdot}OH + SOCl_2 \longrightarrow R{\cdot}CO{\cdot}Cl + SO_2 + HCl.$$

Chlorides of sulphur are also used, and a method patented in U.S.A. consists in mixing the sodium salt with sulphur and passing in chlorine.

2. By the action of chlorine upon the aldehydes in the absence of water: $CH_3{\cdot}CHO + Cl_2 = CH_3{\cdot}COCl + HCl.$

Properties.—The acid chlorides are suffocating liquids which fume in the air, distil without decomposition, and are recon-

verted by water, in many cases at the ordinary temperature, into the corresponding acids and hydrochloric acid:



$$CH_3\cdot CO\cdot Cl + H_2O \rightarrow CH_3\cdot CO\cdot OH + HCl.$$

They are thus more readily decomposed than the alkyl chlorides. When the chlorides are warmed with alcohols, the chlorine is replaced by alkyloxy groups, *e.g.* OCH_3, OC_2H_5, and in this way esters are formed. With ammonia they yield acid amides, $R\cdot CO\cdot NH_2$. With the sodium salts of the fatty acids they yield acid anhydrides. With organo-magnesium compound they first form ketones, and then tertiary alcohols (see p. 75). With silver cyanide acyl cyanides (*e.g.* $CH_3\cdot CO\cdot CN$, acetyl cyanide) are formed, and these on hydrolysis with concentrated hydrochloric acid yield ketonic acids, $CH_3\cdot CO\cdot COOH$.

The acid chlorides can be regarded as aldehydes in which the hydrogen atom of the $\cdot CH:O$ group has been replaced by chlorine. As such they can be reduced to the aldehydes, and the most convenient method appears to consist in passing a current of hydrogen into a hot xylene solution of the chloride containing palladinized barium sulphate in suspension as catalyst. (*Rosemund*, B., 1918, **51**, 585; 1922, **55**, 2357, 2888.)

Formyl chloride is not known.

Acetyl chloride (*Ethanoyl chloride*), $CH_3\cdot COCl$, is a mobile, colourless liquid of suffocating odour. Boils at 55°, has a sp. gr. 1·13 at 0°, reacts extremely vigorously with water and ammonium hydroxide, and is a reagent of exceptional importance, since it serves for the conversion of the alcohols and primary and secondary amines into their acetyl derivatives. It is thus frequently used for detecting OH, NH_2 or NH groups in organic compounds. The compound under examination is heated with acetyl chloride (or even better, acetic anhydride), and the pure product either analysed or hydrolysed, and acetic acid tested for in the products of hydrolysis (see p. 209).

With hydroxyl compounds the H of the OH becomes replaced by the acetyl group and a compound $R\cdot O\cdot CO\cdot CH_3$, is obtained; from alcohols the alkyl acetates (esters) are thus formed. The $\cdot O\cdot CO\cdot CH_3$ group present in such compounds is termed **acetoxyl**.

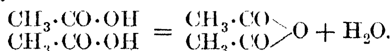
When several hydroxyl groups are present in a molecule, as in glycerol, it frequently happens that most of these

become replaced by acetoxyl and one by chlorine and hence completely to acetylate, such a compound acetic anhydride is preferable to acetyl chloride.

Acid bromides and iodides are known and closely resemble the chlorides. Their boiling-points are higher.

C. Acid Anhydrides

Corresponding with the monobasic fatty acids there are anhydrides, which may be regarded as derived from two molecules of the acid by the elimination of a molecule of water, *e.g.*:



$$\begin{matrix} CH_3\cdot CO\cdot OH \\ CH_3\cdot CO\cdot OH \end{matrix} = \begin{matrix} CH_3\cdot CO \\ CH_3\cdot CO \end{matrix}\!\!>\!O + H_2O.$$

They may also be considered as **acyl oxides.** For instance, $(CH_3\cdot CO)_2O$ = **acetyl oxide.**

Preparation.—1. They cannot, as a rule, be obtained by the direct withdrawal of water from the acids, but by the action of acid chlorides upon the alkali salts of the acids:

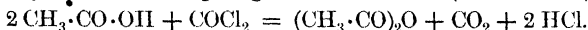


$$CH_3\cdot CO\cdot Cl + Na\,O\cdot CO\cdot CH_3 = (CH_3\cdot CO)_2O + NaCl.$$

A very convenient method for preparing them is by the action of phosphorus oxychloride on the sodium salts of the acids, care being taken that sufficient of the dry sodium salt is used to decompose the acid chloride first formed (see p. 185).

Thionyl chloride can be used instead of $POCl_3$, an intermediate product, $(R\cdot CO\cdot O)_2SO$, is formed, and this breaks up into SO_2 and $(R\cdot CO)_2O$ when heated, or with excess of $SOCl_2$ it yields SO_2 and $R\cdot COCl$. (*Denham* and *Woodhouse*, J. C. S. 1913, **103**, 1861.)

2. By the action of phosgene on the acids (B. **17**, 1286):



$$2\,CH_3\cdot CO\cdot OH + COCl_2 = (CH_3\cdot CO)_2O + CO_2 + 2\,HCl.$$

3. The anhydrides of the higher acids are often prepared by the action of acetic anhydride on their sodium salts.

Properties.—The majority of the acid anhydrides are liquids, but those of higher molecular weight solids, of neutral reaction, and soluble in alcohol and ether. They are non-miscible with water, but are gradually hydrolysed by it to the free acids. Dilute alkalis decompose them readily. When warmed with alcohols they yield esters; with ammonia, acid amides; and with hydrogen chloride, free acid and acid chloride:



$$(CH_3\cdot CO)_2O + HCl = CH_3\cdot CO\cdot Cl + CH_3\cdot CO\cdot OH.$$

The boiling-points follow the order:
$R \cdot CO \cdot Cl < R \cdot CO \cdot OEt < R \cdot CO \cdot OH < (R \cdot CO)_2O < R \cdot CO \cdot NH_2$.
Compare analogous alkyl compounds.

Acetic anhydride $(CH_3 \cdot CO)_2O$, is a mobile liquid of suffocating odour, boiling at 137°, and having a sp. gr. of 1·073 at 20°. Like acetyl chloride it is a reagent of great importance, and is largely made use of in testing for and estimating hydroxyl groups in carbon compounds, and for converting hydroxy-, amino- and imino- compounds into acetyl derivatives, *e.g.* for manufacturing acetylcellulose for artificial silk. A catalytic method of manufacture consists in passing dry acetic acid vapour over dry BaO or ZnO at 250°–300° and fractionating the product.

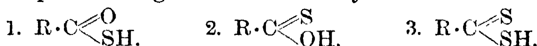
In preparing acetyl derivatives by means of the anhydride a small amount of a catalyst, *e.g.* concentrated sulphuric acid is frequently used.

Mixed anhydrides containing two different acyl groups are also known (*Gerhardt*, *Williamson*), *e.g.* $C_2H_3O \cdot O \cdot OC_5H_{11}$. When distilled they yield the two simple anhydrides.

Acyl peroxides have also been prepared. **Acetyl peroxide**, $(C_2H_3O)_2O_2$, is a thick liquid insoluble in water; it acts as a strong oxidizing agent, explodes when heated, and is prepared by the action of barium peroxide, BaO_2, upon acetic anhydride. Numerous other **peroxides** have been prepared by *Baeyer* and *Villiger* (B. 1901, **34**, 738) by means of hydrogen peroxide in the presence of potassium hydroxide. Among the simpler of these peroxides may be mentioned **ethyl hydrogen peroxide**, $C_2H_5 \cdot O \cdot O \cdot H$, a colourless liquid; **diethyl peroxide**, $C_2H_5 \cdot O \cdot O \cdot C_2H_5$, a liquid boiling at 65°; **acetone peroxide**, $(C_3H_6O_2)_2$, boiling at 132°; and **triacetone peroxide**, $(C_3H_6O_2)_3$, melting at 97°. Many of these compounds are explosive.

D. Thio-acids and Thio-anhydrides

The sulphur analogues of the carboxylic acids are:

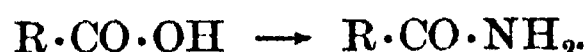


Known respectively as thiolic, thionic, and thion-thiolic acids.

Thiacetic acid (*Ethane-thiolic acid*), $CH_3 \cdot CO \cdot SH$, is a colourless liquid boiling below 100°; it smells of acetic acid and sulphuretted hydrogen, and is readily decomposed by water into these two components. It is prepared from acetic acid and phosphorus pentasulphide, P_2S_5. The other thio-compounds are likewise readily hydrolysed, yielding acetic acid and hydrogen sulphide.

E. Acid Amides and Hydrazides

Amides.—An acid amide is the compound derived from the acid by the introduction of the amido* group in place of the hydroxyl radical of the carboxylic group:



$$R\cdot CO\cdot OH \rightarrow R\cdot CO\cdot NH_2.$$

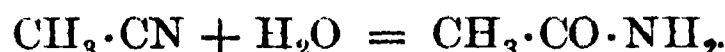
They may also be regarded as derived from ammonia by the replacement of a hydrogen atom by an acyl group, *e.g.* $NH_2\cdot CO\cdot CH_3$. **Secondary** and **tertiary amides,** *e.g.* $NH(CO\cdot CH_3)_2$, and $N(CO\cdot CH_3)_3$, are known, but are of relatively small importance.

Modes of Formation. — 1. By the dry distillation of the **ammonium salts of the fatty acids:**



$$CH_3\cdot CO\cdot ONH_4 = CH_3\cdot CO\cdot NH_2 + H_2O.$$

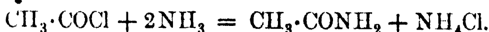
2. By addition of water to the alkyl cyanides (nitriles):



$$CH_3\cdot CN + H_2O = CH_3\cdot CO\cdot NH_2.$$

This addition of water is frequently effected by dissolving the nitrile in concentrated sulphuric acid, or in acetic and concentrated sulphuric acids, or by shaking with concentrated hydrochloric acid in the cold; also, and often quantitatively, by hydrogen peroxide, H_2O_2, in alkaline solution. In some cases a further addition of water occurs, and the ammonium salt of the acid is formed.

3. By the action of acid chlorides or acid anhydrides upon aqueous ammonia or solid ammonium carbonate; if amines are employed here, in place of ammonia, **alkylated amides** are formed:



$$CH_3\cdot COCl + 2NH_3 = CH_3\cdot CONH_2 + NH_4Cl.$$

4. By heating esters with ammonia solution, sometimes even on shaking in the cold:



$$CH_3\cdot CO\cdot OC_2H_5 + NH_3 = CH_3\cdot CO\cdot NH_2 + C_2H_5OH.$$

Properties.—1. With the exception of formamide they are colourless crystalline compounds, volatile without decomposition, but with relatively high boiling-points. The following

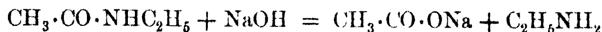
* *The* NH_2 *group is usually termed an* amino *group when present in a primary amine, but an* amido *group when present in an acid amide.*

comparison of boiling-points is interesting, as the order is the same for most groups:—

	Acetyl chloride.	Ethyl acetate.	Acetic acid.	Acetic anhydride.	Acetamide.
Boiling-point	55°	78°	117°	137°	222°

2. The lower members are soluble in water, and although derivatives of ammonia are, unlike most amines, practically neutral, the strongly positive character of the hydrogen atoms of the ammonia being cancelled by the entrance of the negative acyl radical. Still, the primary amides are capable of forming additive compounds with some acids, *e.g.* acetamide yields the compound $(C_2H_3O\cdot NH_2)_2HCl$, "**acetamide hydrochloride**"; these are, however, unstable, and are decomposed for the most part by water alone. On the other hand, the hydrogen of the amido group can be replaced by particular metals, especially mercury (also sodium; cf. B. **23**, 3037; **28**, 2353), the amides, therefore, playing the part of weak acids in the compounds so obtained, *e.g.* **mercury acetamide**, $(CH_3\cdot CONH)_2Hg$.

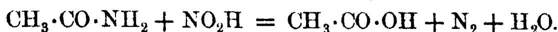
3. The amides are readily hydrolysed, more especially by alkalis, to the free acid and ammonia. Alkylated amides on hydrolysis yield the acid (or sodium salt) and an amine (not ammonia). Amines are not decomposed by alkalis.



$$CH_3\cdot CO\cdot NHC_2H_5 + NaOH = CH_3\cdot CO\cdot ONa + C_2H_5NH_2$$

Hydrolysis of Acid Amides.—The velocity of hydrolysis of the amides of the common fatty acids has been determined by *Crocker* and *Lowe* (J. C. S. 1907, **91**, 593 and 952), using an electro-conductivity method. With sodium hydroxide and also hydrochloric acid, formamide is hydrolysed most readily, and valeramide least readily.

4. Nitrous acid converts the primary amides into the corresponding acids, with liberation of nitrogen:



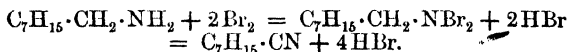
$$CH_3\cdot CO\cdot NH_2 + NO_2H = CH_3\cdot CO\cdot OH + N_2 + H_2O.$$

This reaction is a general one, and corresponds exactly with the action of nitrous acid upon the primary amines (p. 111).

5. Nitriles (see p. 104) are formed by heating with P_4O_{10}, P_2S_5, and PCl_5 (see pp. 192 and 193).

6. If bromine in the presence of alkali is allowed to act upon primary amides, bromamides, $R\cdot CO\cdot NHBr$, *e.g.* $CH_3\cdot CO\cdot NHBr$, **aceto-bromamide** (colourless rectangular plates), are first formed, and these are decomposed by the alkali into

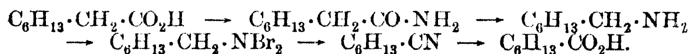
a primary amine, carbon dioxide and potassium hydroxide. If less bromine is used, urea derivatives are formed, *e.g.* methyl acetyl-urea, $CH_3 \cdot NH \cdot CO \cdot NH \cdot CO \cdot CH_3$, which react with excess of alkali, yielding primary amines—in this case $CH_3 \cdot NH_2$—containing 1 atom of carbon less than the original amide. This is an excellent method for the preparation of amines from C_1 to C_5, but less valuable for those from C_6 onwards, as in the case of the higher compounds the production of amine diminishes, a nitrile being formed instead by the further action of the bromine (see below). Such nitriles $C_nH_{2n+1} \cdot CN$, in which $n > 4$, can therefore be obtained directly from the amine by the action of bromine and alkali upon it, thus:—



$$C_7H_{15} \cdot CH_2 \cdot NH_2 + 2Br_2 = C_7H_{15} \cdot CH_2 \cdot NBr_2 + 2HBr$$
$$= C_7H_{15} \cdot CN + 4HBr.$$

(Reversal of the *Mendius* reaction, p. 109; cf. *Hofmann*, B. **15**, 407, 752; **17**, 1407, 1920; **18**, 2737.)

Since these nitriles on hydrolysis yield acids containing 1 atom of carbon less than the amide originally taken, this reaction renders it possible to descend in the series successively from one acid to another (compare p. 166), *e.g.*:



$$C_6H_{13} \cdot CH_2 \cdot CO_2H \longrightarrow C_6H_{13} \cdot CH_2 \cdot CO \cdot NH_2 \longrightarrow C_6H_{13} \cdot CH_2 \cdot NH_2$$
$$\longrightarrow C_6H_{13} \cdot CH_2 \cdot NBr_2 \longrightarrow C_6H_{13} \cdot CN \longrightarrow C_6H_{13} \cdot CO_2H.$$

This has been done in the case of the normal acids from C_{14} to C_1, and it furnishes a further proof of their normal constitution.

Constitution.—Most of the methods of formation and many of the properties of the amides point to the constitutional formula (I). A second formula is possible (II), in favour of which certain arguments have been adduced (B. **22**, 3273; **23**, 103; **25**, 1435):

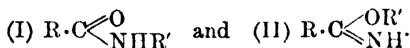


$$\text{(I) } R \cdot C \begin{matrix} \diagup O \\ \diagdown NH_2 \end{matrix} \qquad \text{(II) } R \cdot C \begin{matrix} \diagup OH \\ \diagdown NH \end{matrix}$$

This last formula easily passes into the first by the migration of a hydrogen atom, and most of the reactions of the simple amides are explicable almost equally well by either formula. (Cf. *Titherley*, J. C. S. 1897, 468; 1901, 407.)

We thus have a single compound which appears to possess, according to its reactions, two distinct formulæ. Such a substance is usually termed a **tautomeric substance.**

On alkylation, under different conditions, it is possible to obtain two distinct types of mono-alkylated amides, viz.:



These differ as regards physical and chemical properties; they are isomeric. Compounds of type I closely resemble the original amides; compounds of type II are usually known as **imino ethers**, and differ to a large extent (p. 194).

In many other cases we find that a tautomeric substance gives rise to two distinct groups of alkyl derivatives (see Cyanogen Derivatives, also Chap. XLVII, G.).

Formamide (*Methane-amide*), $HCO \cdot NH_2$, is a liquid readily soluble in water and alcohol. It boils with partial decomposition at about 200°. When quickly heated it decomposes into CO and NH_3, and with phosphorus pentoxide it yields hydrocyanic acid.

Acetamide, *Ethane-amide*, $CH_3 \cdot CO \cdot NH_2$, forms long needles, readily soluble in water and alcohol. It melts at 82°, boils at 222°, and when pure has no odour.

Di-acetamide, $(C_2H_3O)_2NH$. M.-pt. 78°; b.-pt. 223°.

HYDRAZIDES

Just as ammonia by the introduction of acyl groups yields the acid amides, so hydrazine yields the **acid hydrazides**, *e.g.* acetyl hydrazine or **acet-hydrazide**, $CH_3 \cdot CO \cdot NH \cdot NH_2$. They are formed by the action of esters on hydrazine. They are basic in character, are readily hydrolysed, and possess reducing properties. With nitrous acid they yield **acid azides**, *e.g.* $CH_3 \cdot CO \cdot N\langle{N \atop N}$ (with N=N double bond), which are acyl derivatives of hydrazoic acid, (N_3H). (Cf. Curtius, J. pr., 1916, **94**, 273; 1917, **95**, 168, 327.)

All 4 hydrogen atoms in hydrazine can be replaced by acyl radicals in much the same manner as the 3 hydrogen atoms in the ammonia molecule can. The products are termed di-, tri-, and tetra-hydrazides, *e.g.* tetra-acet-hydrazide, $Ac_2N \cdot NAc_2$.

F. Amido-chlorides and Imido-chlorides

By the action of PCl_5 upon the primary amides an exchange of Cl_2 for O takes place, giving rise in the first instance to the so-called **amido-chlorides**, *e.g.* **acetdichloroamide**,

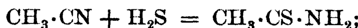
$CH_3 \cdot CCl_2 \cdot NH_2$; these are extremely unstable compounds, being converted by water into amide and hydrochloric acid, and readily giving up HCl, with formation of **imido-chlorides**, *e.g.* $CH_3 \cdot CCl:NH$, **acetchloroimide.** The imido-chloroides are also relatively unstable, yielding with water the amide and hydrochloric acid. When heated, they break up into nitrile and hydrochloric acid.

The alkylated amides (p. 189) also yield chloroamides, *e.g.* $CH_3 \cdot CO \cdot NH \cdot C_2H_5$ gives $CH_3 \cdot CCl_2 \cdot NH \cdot C_2H_5$, **ethyl acetchloroamide,** and $CH_3 \cdot CO \cdot NR_2$ gives $CH_3 \cdot CCl_2 \cdot NR_2$; if these still contain amido-hydrogen, they readily yield imido-chlorides, *e.g.* $CH_3 \cdot CCl:N \cdot C_2H_5$, **ethyl acetchloroimide.**

The chlorine in these compounds is chemically active; it can be exchanged for sulphur or for an amino group.

G. Thiamides and Imino-thio-ethers

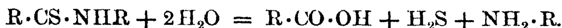
Thiamides are compounds derived from the amides by the exchange of oxygen for sulphur, *e.g.* $CH_3 \cdot CS \cdot NH_2$, **thiacetamide** (*ethane-thion-amide*), $CH_3 \cdot CS \cdot NHC_6H_5$, **thiacetanilide.** They are mostly crystalline compounds, and are formed by the **addition of H_2S to the nitriles** (*Cahours*), *e.g.*:



$$CH_3 \cdot CN + H_2S = CH_3 \cdot CS \cdot NH_2;$$

by treating acid amides with P_2S_5; from the amido-chlorides, as given above; and by the action of H_2S or CS_2 upon the amidines. Both simple and alkylated thiamides are known.

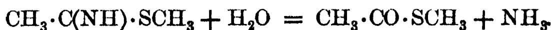
When heated alone, they yield a nitrile and sulphuretted hydrogen (compare Elimination of Water from Amides). When hydrolysed with alkalis, they yield the corresponding acid, ammonia (amine) and H_2S, thus:—



$$R \cdot CS \cdot NHR + 2H_2O = R \cdot CO \cdot OH + H_2S + NH_2 \cdot R.$$

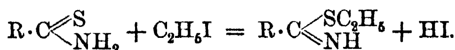
They are rather more acid in character than the amides, and thus many of them are soluble in alkali and yield metallic derivatives. Consequently, for them, as well as for the amides, the iso-formula $R \cdot C \genfrac{}{}{0pt}{}{\diagup SH}{\diagdown NH}$ is taken into consideration. From this pseudo form $R \cdot C \genfrac{}{}{0pt}{}{\diagup SH}{\diagdown NH}$, **iso-thio acid amides,** are derived a number of compounds, the **Imino-thio-ethers,** by the replacement of one or both the hydrogen atoms by alkyl groups,

acetimido-thiomethyl, $CH_3 \cdot C \begin{smallmatrix} S \cdot CH_3 \\ NH \end{smallmatrix}$; **methyl iso-thio-acet-anilide**, $CH_3 \cdot C \begin{smallmatrix} S \cdot CH_3 \\ N \cdot C_6H_5 \end{smallmatrix}$. They are decomposed by hydrochloric acid into esters of thiacetic acid, thus:—



$$CH_3 \cdot C(NH) \cdot SCH_3 + H_2O = CH_3 \cdot CO \cdot SCH_3 + NH_3.$$

These imino-thio-ethers are prepared by the action of mercaptans upon nitriles in presence of hydrochloric acid gas (*Pinner*), and by the action of alkyl iodides upon thiamides (*Wallach, Bernthsen*):

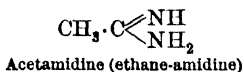


$$R \cdot C \begin{smallmatrix} S \\ NH_2 \end{smallmatrix} + C_2H_5I = R \cdot C \begin{smallmatrix} SC_2H_5 \\ NH \end{smallmatrix} + HI.$$

Imino-ethers, $R \cdot C \begin{smallmatrix} NH \\ OR' \end{smallmatrix}$, which are the oxygen compounds corresponding with the above imino-thio-ethers, and which are isomeric with the alkylated amides, are also known (*Pinner*). They are derived from the pseudo form of the acid amides, $R \cdot C \begin{smallmatrix} NH \\ OH \end{smallmatrix}$, hypothetical compounds unknown in the free state, which are isomeric with the simple amides. They are formed by the combination of a nitrile with an alcohol under the influence of hydrochloric acid gas, and in certain cases by alkylating amides; some of them are liquids which boil without decomposition, but others are only known in the form of salts.

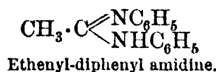
H. Amidines

Amidines are compounds derived from the amides, $R \cdot CO \cdot NH_2$, $R \cdot CO \cdot NHR'$, and $R \cdot CO \cdot NR'_2$, by the replacement of oxygen by the bivalent imido-residue NH or (NR):



$$CH_3 \cdot C \begin{smallmatrix} NH \\ NH_2 \end{smallmatrix}$$

Acetamidine (ethane-amidine)

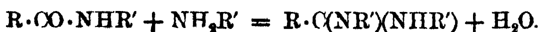


$$CH_3 \cdot C \begin{smallmatrix} NC_6H_5 \\ NHC_6H_5 \end{smallmatrix}$$

Ethenyl-diphenyl amidine.

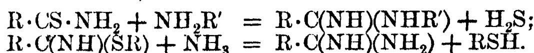
The amidines are well-defined crystalline bases, and form stable salts. Like all acyl derivatives, they are readily hydrolysed, and thus differ from the amines.

Formation.—1. By heating the amides with amines in presence of PCl_3 (*Hofmann*):



$$R \cdot CO \cdot NHR' + NH_2R' = R \cdot C(NR')(NHR') + H_2O.$$

2. By treating the imido-chlorides, thiamides, and iso-thiamides with ammonia or with primary or secondary amines (*Wallach*, *Bernthsen*), thus:—



$$R{\cdot}CS{\cdot}NH_2 + NH_2R' = R{\cdot}C(NH)(NHR') + H_2S;$$
$$R{\cdot}C(NH)(SR) + NH_3 = R{\cdot}C(NH)(NH_2) + RSH.$$

3. By heating the nitriles with (primary or secondary) amine hydrochloride; this is a particularly easy method when aromatic amines are used, but not in the case of ammonium chloride (*Bernthsen*):



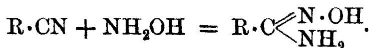
$$CH_3{\cdot}CN + NH_2{\cdot}R = CH_3{\cdot}C(NH)(NHR).$$

4. By the action of amine bases or ammonia upon imino-ethers.

Behaviour.—1. They decompose into ammonia or amine and acid when boiled with acids or alkalis (see above), and into ammonia and amide upon boiling with water.

2. The dry compounds, when heated, readily yield ammonia or amine and acid nitrile, so long as the imido-hydrogen atom has not been replaced by alkyl groups.

Amidoximes are the compounds formed by the addition of hydroxylamine to nitriles, and, from this mode of formation and from their properties, appear to be amidines in which an amido- (imido-) hydrogen atom is replaced by hydroxyl:



$$R{\cdot}CN + NH_2OH = R{\cdot}C{<}^{N{\cdot}OH}_{NH_2}.$$

Such an amidoxime is, for instance, **isuret**, $NH_2{\cdot}CH{:}N{\cdot}OH$, also termed methenyl amidoxime, which is prepared from hydrocyanic acid and hydroxylamine; it is isomeric with carbamide or urea; also **ethenyl amidoxime**, $CH_3{\cdot}C(N{\cdot}OH)(NH_2)$. These compounds are hydrolysed in much the same manner as amidines.

VIII. POLYHYDRIC ALCOHOLS

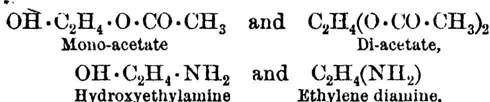
A. Dihydric Alcohols or Glycols, $C_nH_{2n}(OH)_2$

The dihydric alcohols may be regarded as derived from the paraffins by the replacement of *two* hydrogen atoms by two hydroxyl groups.

As the monohydric alcohols are often compared with the hydroxides derived from the monovalent metals, we may

compare the glycols with the hydroxides derived from the bivalent metals, *e.g.* $C_2H_4(OH)_2$ with $Pb(OH)_2$. In the saturated dihydric alcohols we have the hydroxyl groups attached to a bivalent **alkylene** radical, *e.g.* C_2H_4'', C_3H_6'', &c.

In many respects they resemble the monohydric alcohols, but they possess these properties in duplicate. Just as, *e.g.*, plumbous hydroxide, $Pb(OH)_2$, can give rise to two series of salts, *e.g.* the basic chloride, $OH \cdot Pb \cdot Cl$, and the normal chloride, $PbCl_2$, so glycol, $C_2H_4(OH)_2$, can give rise to two chlorides, $OH \cdot C_2H_4 \cdot Cl$ and $C_2H_4Cl_2$, known respectively as glycol monochlorhydrin and glycol dichlorhydrin or ethylene dichloride. Similarly, with the acetates and amines derived from glycol we have—



$OH \cdot C_2H_4 \cdot O \cdot CO \cdot CH_3$ (Mono-acetate) and $C_2H_4(O \cdot CO \cdot CH_3)_2$ (Di-acetate),

$OH \cdot C_2H_4 \cdot NH_2$ (Hydroxyethylamine) and $C_2H_4(NH_2)$ (Ethylene diamine),

and similarly with other glycols.

The glycols, as alcohols, give rise to every class of alcoholic derivative; but when, for example, the formation of an ester such as glycollic monoacetate has taken place, this still behaves as a monohydric alcohol, yielding, *e.g.*, with a second molecule of acid, a new ester; it is therefore termed an **ester-alcohol**.

It is not necessary that both the groups which replace the hydrogen or hydroxyl should be of the same nature; thus we know a mixed derivative of the composition $NH_2 \cdot C_2H_4 \cdot SO_2 \cdot OH$, which possesses at one and the same time the character of an amine and of a sulphonic acid.

The glycols are mostly thick liquids of sweetish taste, a few only being solid crystalline compounds; they dissolve readily in water and alcohol, but are only sparingly soluble in ether. It will be found that the solubility of a compound in water tends to increase, and its solubility in ether to decrease, with the number of hydroxyl groups present in the molecule of the compound. Their boiling-points are much higher than those of the corresponding monohydric alcohols, just as these latter possess considerably higher boiling-points than the hydrocarbons from which they are derived.

Constitution.—As already stated, the glycols contain two hydroxyl groups in each molecule; the arguments in favour of the presence of these hydroxyl groups are exactly similar to those used in the study of the constitution of ethyl alcohol,

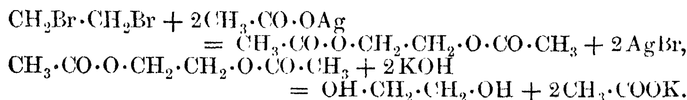
and are based mainly on certain methods of formation, and on the chief chemical characteristics of the compounds.

Glycols which contain two hydroxyls linked to the same carbon atom are, as a rule, incapable of existence, and are only known in derivatives (see p. 67). Instead of the glycols $CH_2(OH)_2$ and $CH_3{\cdot}CH(OH)_2$, we always obtain the corresponding aldehydes, $CH_2{:}O$ and $CH_3{\cdot}CH{:}O$. All glycols contain their hydroxyls attached to two different carbon atoms. Glycol itself has thus the constitution $OH{\cdot}CH_2{\cdot}CH_2{\cdot}OH$, which can be proved directly by transforming it, by means of hydrochloric acid, into glycol chlorhydrin, $CH_2Cl{\cdot}CH_2{\cdot}OH$, and oxidizing the latter to monochloracetic acid, $CH_2Cl{\cdot}CO{\cdot}OH$. In this last compound the chlorine and hydroxyl are united to different carbon atoms, and consequently the same applies to glycol chlorhydrin and to the two hydroxyl groups of glycol.

The monohydric alcohols are distinguished as primary, secondary, and tertiary. The glycols may in the same way be characterized as **di-primary** when they contain the group $CH_2{\cdot}OH$ twice, as in glycol; as **primary-secondary** when they contain the group $CH_2{\cdot}OH$ together with the group $CH{\cdot}OH$, as in propylene glycol, $CH_3{\cdot}CH(OH){\cdot}CH_2OH$; further as **di-secondary**, **primary-tertiary**, **secondary-tertiary**, and **di-tertiary**. The structure of a glycol is usually determined by an examination of its oxidation products. (See pp. 199, 210, *et seq.*)

Modes of Formation.—1. From the di-halogen-substituted derivatives of the paraffins, in which the two halogen atoms are attached to two different carbon atoms, *e.g.* ethylene bromide:

(*a*) By transformation into the di-acetates by means of silver or potassium acetate, and hydrolysis of the ester so produced by potash, baryta, or alcoholic sodium ethoxide (*Bainbridge*, J. C. S. 1914, **105**, 2291):

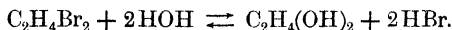


$$CH_2Br{\cdot}CH_2Br + 2CH_3{\cdot}CO{\cdot}OAg = CH_3{\cdot}CO{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}CO{\cdot}CH_3 + 2AgBr,$$

$$CH_3{\cdot}CO{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}O{\cdot}CO{\cdot}CH_3 + 2KOH = OH{\cdot}CH_2{\cdot}CH_2{\cdot}OH + 2CH_3{\cdot}COOK.$$

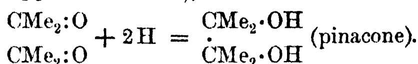
In the actual preparation of glycol from ethylene bromide, potassium acetate, and alcohol (*Demole*), this saponification ensues directly upon prolonged boiling of the mixture.

(*b*) By boiling with water and lead oxide or potassium carbonate. These reagents serve to neutralize the acid as it is formed, and so the reaction is facilitated:



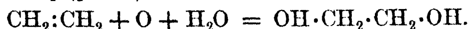
$$C_2H_4Br_2 + 2HOH \rightleftarrows C_2H_4(OH)_2 + 2HBr.$$

2. In the reduction of ketones to secondary alcohols, the so-called pinacones, *i.e.* di-tertiary glycols, are obtained as by-products (see pp. 75 and 141), thus:—



$$\begin{matrix} CMe_2{:}O \\ CMe_2{:}O \end{matrix} + 2H = \begin{matrix} CMe_2{\cdot}OH \\ \cdot \\ CMe_2{\cdot}OH \end{matrix} \text{ (pinacone).}$$

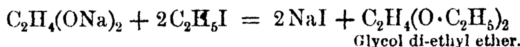
3. By the careful oxidation of olefines by means of very dilute $KMnO_4$ (p. 48):



$$CH_2{:}CH_2 + O + H_2O = OH{\cdot}CH_2{\cdot}CH_2{\cdot}OH.$$

Behaviour.—1. As in the case of the monohydric alcohols, the hydrogen of the hydroxylic groups is directly replaceable by potassium or sodium, with the formation of **alcoholates**, *e.g.* $OH{\cdot}C_2H_4{\cdot}ONa$ and $C_2H_4(ONa)_2$, **sodium and di-sodium glycols.**

2. The metal in these compounds may be exchanged for new alkyl groups by treatment with alkyl iodide, when glycollic ethers are obtained:



$$C_2H_4(ONa)_2 + 2C_2H_5I = 2NaI + C_2H_4(O{\cdot}C_2H_5)_2$$
Glycol di-ethyl ether.

These ethers, like those of the monohydric alcohols, are stable, and cannot be hydrolysed by dilute mineral acids or alkalis.

3. Acids act upon them to produce esters, which are either normal esters or ester-alcohols (see p. 196).

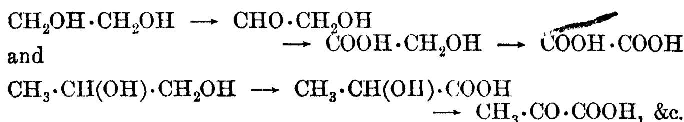
The halogen esters of the glycols are termed chlor-, brom-, or iodhydrins, *e.g.* glycol chlorhydrin, $C_2H_4Cl(OH)$, glycol di-chlorhydrin, $C_2H_4Cl_2$, &c. The ester-alcohols which are formed by the action of halogen hydride may also be regarded as mono-substitution products of the monohydric alcohols, which cannot be prepared by direct chlorination, *e.g.* $C_2H_4Cl(OH)$, monochlorethyl alcohol. Similarly the di-halogen esters, $CH_2Cl{\cdot}CH_2Cl$, $CH_2Br{\cdot}CH_2Br$, &c., are the di-substitution products of the paraffins, viz. ethylene dichloride and dibromide.

4. As the halogen atoms in the chlor-, brom-, and iodhydrins are readily replaceable, just as in C_2H_5Cl or C_2H_5I, these compounds may be used for the preparation of most of the other glycol derivatives; thus they yield thio-glycols with potassium hydrosulphide, amines with ammonia, sulphonic acids with sodium bisulphite, and nitriles with potassium cyanide.

5. Alkalis react with the glycol monochlorhydrins, and by the elimination of HCl yield cyclic anhydrides, *e.g.* **ethylene oxide,** $\begin{matrix} CH_2 \\ \cdot \\ CH_2 \end{matrix}\!\!>\!O$. It is interesting to note that these anhydrides

cannot be obtained by the elimination of water from the glycols themselves. When ethylene glycol is heated with zinc chloride at 230° water is eliminated, and the product obtained is acetaldehyde (or a polymer). This reaction is explained by assuming the intermediate formation of unsaturated alchohols which are not in themselves capable of existence, *e.g.* $CH_2{:}CH(OH)$, but which immediately undergo transformation into the isomeric aldehydes or ketones: $CH_2{:}CH{\cdot}OH = CH_3{\cdot}CH{:}O$.

6. As alcohols the glycols are readily oxidized. If they contain the primary alcoholic group, they can yield aldehydes and acids containing the same number of carbon atoms. If they contain a secondary alcoholic group, they yield ketones, *e.g.*:



$$CH_2OH{\cdot}CH_2OH \rightarrow CHO{\cdot}CH_2OH \rightarrow COOH{\cdot}CH_2OH \rightarrow COOH{\cdot}COOH$$

and

$$CH_3{\cdot}CH(OH){\cdot}CH_2OH \rightarrow CH_3{\cdot}CH(OH){\cdot}COOH \rightarrow CH_3{\cdot}CO{\cdot}COOH, \&c.$$

Methylene- and **Ethylidene-glycol.** (See Aldehydes.)

Ethylene glycol (*glycol*), $OH{\cdot}CH_2{\cdot}CH_2{\cdot}OH$ (*Wurtz*, A. **100**, 110), is prepared from Ethylene bromide by means of potassium acetate in alcoholic solution (*Demole*), or of potassium carbonate in aqueous solution, as given above (A. **192**, 250). For properties, see above. Its formula has been corroborated by the determination of its vapour density. Oxidizing agents transform it into glycollic acid, $OH{\cdot}CH_2{\cdot}CO{\cdot}OH$, and oxalic acid, $OH{\cdot}CO{\cdot}CO{\cdot}OH$. The mono-ethyl, mono-acetyl and diacetyl derivatives are used as solvents in the lacquer (nitrocellulose) industry.

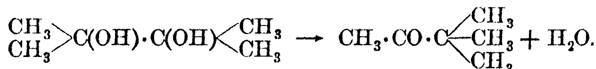
Propylene glycol is known in two isomeric forms, viz.

(*a*) **Trimethylene glycol, β-Propylene glycol,** *Propane*-1 : 3-*diol*, $OH{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}OH$, which is prepared from trimethylene bromide, and is a di-primary glycol boiling at 216°. It is also produced by the *Schizomycetes* fermentation of glycerol (B. **14**, 2270; **54** B, 3115).

(*b*) **α-Propylene glycol,** *Propane*-1 : 2-*diol*, $CH_3{\cdot}CH(OH){\cdot}CH_2{\cdot}OH$, can be prepared from propylene bromide in an analogous manner, but is more easily obtained by distilling glycerol with caustic soda. It boils at 188°. It contains an asymmetric carbon atom in the molecule, and becomes optically (−) active when fermented, *i.e.* fission fungi destroy the dextro modification more rapidly than the laevo.

Four butylene glycols, and various **amylene-** and **hexylene-glycols**, &c., are also known. Of these, the γ-glycols (in which the hydroxyls are in the positions 1:4, and which therefore contain the grouping $\cdot \underset{1}{C}(OH)\cdot \underset{2}{C}\cdot \underset{3}{C}\cdot \underset{4}{C}(OH)\cdot$) yield compounds of the **furane** series by the formation of anhydrides (B. **22**, 2567), and therefore stand in close relation to thiophene and pyrrole, Chap. XXXIV.

Pinacone, Tetramethyl-ethylene glycol (*2:3-Dimethyl-butane-2:3-diol*), $(CH_3)_2:C(OH)\cdot C(OH):(CH_3)_2$. The hydrate, $(+ 6\,H_2O)$, forms large quadratic tables; in the anhydrous state it is a crystalline mass melting at 38° and boiling at 172°. When warmed with dilute sulphuric or hydrochloric acid it yields pinacoline, $CH_3\cdot CO\cdot C(CH_3)_3$, methyl tertiary-butyl ketone or 2:2-dimethyl-butan-3-one (see p. 144):



In this reaction an interesting intramolecular rearrangement occurs, together with the elimination of water.

Numerous other pinacones are known. They may be obtained by reducing ketones or synthetically (*Lieben*, M. **17**, 68; **19**, 16), and with acids yield the corresponding pinacolines.

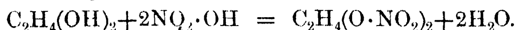
DERIVATIVES OF THE GLYCOLS

The **ethers**, *e.g.* $C_2H_4(OCH_3)_2$, are mostly colourless liquids with ethereal odours, and have lower boiling-points than the glycols. (Cf. Ether and Ethyl Alcohol.) They cannot be readily hydrolysed. The **esters**, *e.g.* $C_2H_4(O\cdot CO\cdot CH_3)_2$, are also mostly liquids, and are readily hydrolysed.

The following esters of inorganic acids are interesting:—

Glycol chlorhydrin, $CH_2Cl\cdot CH_2\cdot OH$, obtained by passing hydrogen chloride into warm glycol, by the addition of hypochlorous acid to ethylene or by the action of ethylene on chlorocarbamide in dilute acetic acid, is a liquid miscible with water, and boiling at 130°; in this last respect differing from its corresponding alcohol to almost the same extent as ethyl chloride does from alcohol.

Glycollic di-nitrate, $C_2H_4(NO_3)_2$, is prepared by acting on glycol with sulphuric and nitric acids:



$$C_2H_4(OH)_2+2NO_2\cdot OH = C_2H_4(O\cdot NO_2)_2+2H_2O.$$

It is a yellowish liquid, insoluble in water, is readily hydro-

lysed by alkalis to glycol and nitric acid, and hence the constitution. The formation of such nitric esters, which are highly explosive, is characteristic of the polyhydric alcohols (see Nitroglycerine).

Ethylene cyanide, $CN \cdot CH_2 \cdot CH_2 \cdot CN$, obtained by the action of potassium cyanide on ethylene dibromide, is a crystalline solid, and on hydrolysis with alkalis yields $CO_2H \cdot CH_2 \cdot CH_2 \cdot CO_2H$, succinic acid, and hence may be regarded as **succinonitrile**.

Glycol monochlorhydrin with potassium cyanide yields **ethylene cyanhydrin**, or the nitrile of β-lactic acid, $OH \cdot CH_2 \cdot CH_2 \cdot CN$. Isomeric with it is **ethylidene cyanhydrin**, $CH_3 \cdot CH(OH) \cdot CN$, the additive product of hydrocyanic acid and aldehyde (p. 132).

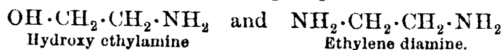
Ethylene oxide, C_2H_4O (*Wurtz*), obtained by distilling glycol chlorhydrin with caustic-potash solution, is a mobile liquid of ethereal odour boiling at 13·5°. It is miscible with water, and slowly converted into the glycol.

It has many of the properties of an unsaturated compound, *e.g.* with HCl it yields the chlorhydrin, with NH_3 the amino alcohol, $OH \cdot CH_2 \cdot CH_2 \cdot NH_2$, with CH_3MgI and then water *n*-propyl alcohol, and with chlorine ethylene dichloride.

It is largely owing to the last reaction that the ring constitution, $\begin{matrix} CH_2 \\ | \\ CH_2 \end{matrix} \!\! > \! O$, and not the open-chain formula, $CH_2{:}CH \cdot OH$, is given to the compound. The formation of additive compounds is accompanied by the rupture of the ring. Some of the higher homologues of ethylene oxide are much more stable, and do not yield additive compounds; this is due to the fact that the ring is more stable and therefore less easy to rupture (compare Polymethylene Compounds).

AMINES OF THE DIHYDRIC ALCOHOLS

These are derived from glycols by the replacement of one or both hydroxyl groups by amino groups:

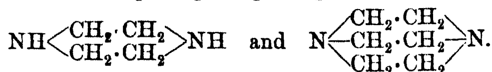


$$OH \cdot CH_2 \cdot CH_2 \cdot NH_2 \quad \text{and} \quad NH_2 \cdot CH_2 \cdot CH_2 \cdot NH_2$$

Hydroxy ethylamine — Ethylene diamine.

In the former case compounds are obtained which possess the properties of an amine in addition to those of an alcohol; in the latter, diamines free from oxygen, which are analogous to ethylamine, but are di-acid and not mono-acid bases.

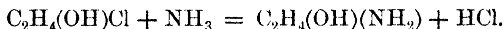
Secondary and **tertiary diamines** corresponding with the **primary amine**, $NH_2\cdot CH_2\cdot CH_2\cdot NH_2$, are known, *e.g.*:



The methods by means of which these diamines can be obtained are analogous to those described for the monamines, viz.:—

1. By heating ethylene bromide, &c., with alcoholic ammonia to 100° (*Hofmann*). The primary, secondary, and tertiary bases, which are formed simultaneously, can be separated by fractional distillation.

The hydroxy amines (or alkines, *Ladenburg*) are obtained in an analogous manner by using ethylene chlorhydrin, thus:—



$$C_2H_4(OH)Cl + NH_3 = C_2H_4(OH)(NH_2) + HCl.$$

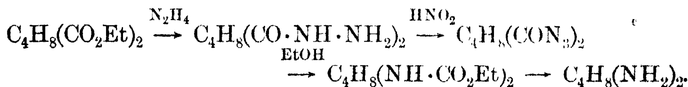
In this case also primary, secondary, and tertiary bases are produced at the same time. Ethylene chlorhydrin yields choline chloride (p. 203) with trimethylamine.

2. Primary diamines are formed by the reduction of the nitriles, $C_nH_{2n}(CN)_2$, with metallic sodium and alcohol, *e.g.*:



$$CN\cdot CH_2\cdot CH_2\cdot CN + 8H = NH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot NH_2.$$

3. From the esters of dibasic acids of the oxalic acid series (p. 239) by converting first into the hydrazide, then into the azide, and through the dicarbamate into the amine (J. pr., 1915 [II], **91**, 1); thus with ethyl adipate:—



$$C_4H_8(CO_2Et)_2 \xrightarrow{N_2H_4} C_4H_8(CO\cdot NH\cdot NH_2)_2 \xrightarrow{HNO_2} C_4H_8(CON_3)_2 \xrightarrow{EtOH} C_4H_8(NH\cdot CO_2Et)_2 \longrightarrow C_4H_8(NH_2)_2.$$

Ethylene diamine, $C_2H_4(NH_2)_2$, **Diethylene diamine**, $(C_2H_4)_2N_2H_2$, &c., are colourless liquids distilling without decomposition. The former boils at 123°, and has an ammoniacal odour; the latter melts at 104° and boils at 146°, and is identical with piperazine, *i.e.* hexahydro-pyrazine. Hence it possesses the constitutional formula $NH<\genfrac{}{}{0pt}{}{CH_2\cdot CH_2}{CH_2\cdot CH_2}>NH$, and has a closed-chain constitution (*Hofmann*, B. **23**, 3297).

Tetramethylene - diamine, *Butane*-1:4-*diamine*, *putrescine*, *butylene-diamine*, $NH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot NH_2$, is prepared according to method 2, and is also formed during the putre-

faction of flesh. As a "γ-diamine", *i.e.* the diamine of a γ-glycol, it is closely related to pyrrole, from which it is formed by the action of hydroxylamine (whereby a dioxime is first produced), and subsequent reduction (B. **22**, 1968).

Pentamethylene diamine, *cadaverine*, $NH_2 \cdot (CH_2)_5 \cdot NH_2$, is formed by the reduction of trimethylene cyanide, $CN \cdot (CH_2)_3 \cdot CN$, which on its part is prepared from trimethylene bromide, $CH_2Br \cdot CH_2 \cdot CH_2Br$, and KCN (*Ladenburg*). It is a colourless, syrupy liquid of very pronounced spermaceti and piperidine odour, solidifies in the cold, and boils at 178°–179°. It possesses especial interest, because, being a δ-diamine, it gives up ammonia and yields the cyclic base **piperidine**, $CH_2{<}\begin{smallmatrix}CH_2 \cdot CH_2\\CH_2 \cdot CH_2\end{smallmatrix}{>}NH$ (see Chap. XXXVII, B.).

Many of these polyacid bases are found in decaying albumen and in corpses, and are designated **ptomaïnes** or **toxines** (cf. *e.g.* B. **19**, 2585).

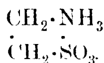
Choline, *bilineurine, ethylol-trimethyl-ammonium hydroxide*, $OH \cdot CH_2 \cdot CH_2 \cdot NMe_3 \cdot OH$ (*Strecker*), is found in the bile (χολή, bile), brain, yolk of egg, &c., being present in these combined with fatty acids and glyceryl-phosphoric acid as lecithin. It is also found in herring brine, hops, beer, and in many fungi, &c., and is obtained by boiling sinapine with alkalis (the old name for this product was "Sincaline"). Choline is a strong, deliquescent base, and readily absorbs carbon dioxide from the air. It is not poisonous. The **chloride** has the formula $OH \cdot C_2H_4 \cdot NMe_3Cl$. Concentrated HNO_3 oxidizes choline to **muscarine**, $C_5H_{15}NO_3 = (OH)_2CH \cdot CH_2 \cdot NMe_3 \cdot OH$, an excessively poisonous base, which is present in toad-stool, *Agaricus muscarius*.

By transforming choline, by means of hydriodic acid, into its iodide, $CH_2I \cdot CH_2 \cdot NMe_3I$, and treating the latter with moist oxide of silver, and also from the putrefaction of choline, **neurine** (νεῦρον, nerve), *trimethyl-vinyl-ammonium hydroxide*, $CH_2{:}CH \cdot NMe_3 \cdot OH$ (*Hofmann*), is obtained. This base, containing the unsaturated radical "vinyl", C_2H_3, is very similar to choline, and can also be prepared from brain substance; it is only known in solution, and is very poisonous. It can be re-transformed into choline. (For this, and also for derivatives, see *e.g.* A. **267**, 249; **268**.)

Another natural compound related to hydroxy ethylamine is **taurine**, $C_2H_7NSO_3$ (*Gmelin*), which is present in combination with cholic acid as **taurocholic acid** in the bile of **oxen**

and many other animals, also in the kidneys, lungs, &c. It crystallizes in large monoclinic prisms, is readily soluble in hot water, but insoluble in alcohol, and decomposes when strongly heated. Its constitution follows from its synthesis.

Isethionic acid, hydroxy-ethyl-sulphonic acid, $OH \cdot CH_2 \cdot CH_2 \cdot SO_2 \cdot OH$, is obtained when carbyl sulphate, $C_2H_4S_2O_6$ (from C_2H_4 and SO_3), is boiled with water; its constitution follows from its properties, and also from the fact that it may be obtained by the oxidation of the hydroxymercaptan, $OH \cdot CH_2 \cdot CH_2 \cdot SH$. Isethionic acid with PCl_5 yields the chloride $CH_2Cl \cdot CH_2 \cdot SO_2Cl$, and this with water gives chloro-ethyl-sulphonic acid, $CH_2Cl \cdot CH_2 \cdot SO_2 \cdot OH$, which with ammonia yields taurine; its constitution must, therefore, be $NH_2 \cdot CH_2 \cdot CH_2 \cdot SO_2 \cdot OH$, **amino-ethyl-sulphonic acid**, and in accordance with this constitution it unites in itself the properties of an alcoholic amine and a sulphonic acid and is therefore at the same time a base and an acid, but the acidic properties predominate. Its reaction with nitrous acid is that of a primary amine. As an alkyl sulphonic acid, it is not hydrolysed by boiling with alkalis and acids. It is sometimes represented as a cyclic ammonium salt,



$$\begin{array}{c} CH_2 \cdot NH_3 \\ CH_2 \cdot SO_3. \end{array}$$

Numerous unsaturated glycols of the type, $OH \cdot CHMe \cdot C \vdots C \cdot CHMe \cdot OH$, have been prepared by the action of aldehydes or ketones on the *Grignard* compounds, $Br.MgC \vdots C \cdot MgBr$, derived from acetylene (*Iocitsch*, Annales, 1913, *VIII*, **30**).

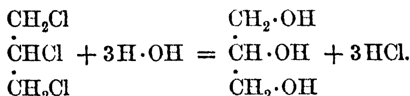
B. Trihydric Alcohols

The molecule of each trihydric alcohol contains three hydroxyl groups, each attached to a different carbon atom. They may be regarded as analogous to the hydroxides of tervalent metals *e.g.* $C_3H_5(OH)_3$ and $Al(OH)_3$. They can give rise to three distinct groups of derivatives according as one, two, or three of the hydroxyls react, *e.g.* chlorides—$C_3H_5Cl(OH)_2$, monochlorhydrin; $C_3H_5Cl_2 \cdot OH$, dichlorhydrin; and $C_3H_5Cl_3$, trichlorhydrin of glycerol. Similarly for acetates, amino-derivatives, &c.

Although the compound $CH(OH)_3$, **ortho-formic acid** is not known, derivatives, *e.g.* **ethyl ortho-formate**, $CH(OEt)_3$, (p. 148), and similarly **ethyl ortho-acetate**, $CH_3 \cdot C(OEt)_3$, can readily be prepared.

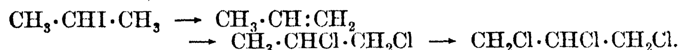
Glycerine, *glycerol*, *propane*-1:2:3-*triol*, $OH \cdot CH_2 \cdot CH(OH) \cdot CH_2 \cdot OH$. (*Scheele*, 1779; formula established by *Pelouze* in 1836, and constitution by *Berthelot* and *Wurtz*.)

Synthesis.—By heating 1:2:3-trichlorpropane with water to 170°:



$$\begin{array}{l} CH_2Cl \\ CHCl \\ CH_2Cl \end{array} + 3H \cdot OH = \begin{array}{l} CH_2 \cdot OH \\ CH \cdot OH \\ CH_2 \cdot OH \end{array} + 3HCl.$$

The trichlorpropane is itself obtainable from isopropyl iodide (which can also be prepared synthetically) by conversion into propylene, addition of Cl_2, and heating the propylene dichloride thus formed with iodine chloride (*Friedel* and *Silva*, Bull. Soc. Chim. **20**, 98):



$$CH_3 \cdot CHI \cdot CH_3 \rightarrow CH_3 \cdot CH{:}CH_2 \rightarrow CH_3 \cdot CHCl \cdot CH_2Cl \rightarrow CH_2Cl \cdot CHCl \cdot CH_2Cl.$$

Glycerol is also produced when allyl alcohol is oxidized with very dilute potassium permanganate:



$$CH_2{:}CH \cdot CH_2 \cdot OH \rightarrow OH \cdot CH_2 \cdot CH(OH) \cdot CH_2 \cdot OH.$$

The *constitution* of glycerol follows from these syntheses and also from its relation to tartronic acid (p. 206); each of the three hydroxyls is attached to a separate carbon atom.

Manufacture.—It is a by-product in the manufacture of hard soaps (p. 164), and crude glycerine is made by concentrating the waste lyes in suitable salting-out evaporators, from which the common salt can be removed as it is formed. It is also a by-product in the manufacture of stearic acid for candles. The oils or fats are hydrolysed by one of the methods mentioned on p. 164, or by means of an enzyme (*lipase*) present in castor seeds. The crude, neutral glycerine liquor, after removal of the fatty acids, is concentrated under reduced pressure as glycerine vaporizes at 100°, and the crude, concentrated product is refined by distillation with superheated steam under reduced pressure, the distillate is again concentrated, and, if necessary, filtered through animal charcoal.

A biochemical method is by the alcoholic fermentation of glucose. In the ordinary fermentation, by means of yeast (p. 79), a 3-per-cent yield of glycerol is obtained, but this is easily increased to 24 per cent by the addition of small amounts of sodium sulphite (*Helv.*, 1919, **2**, 167) or of sodium carbonate at intervals (J. Ind. 1919, **38**, 175 R.).

Properties.—It is a thick, colourless syrup, of specific gravity

1·27, solidifies, when strongly cooled, to crystals, like those of sugar-candy, which melt at 17°. It boils at 290°, but is best distilled under diminished pressure, *e.g.* at 170° under 12 mm. It is very hygroscopic, and mixes with water and alcohol in all proportions, but is insoluble in ether.

Uses.—In the manufacture of liqueurs, fruit preserves, wine, cakes; for non-drying stamp colours and blacking; when mixed with glue, in book printing; as a healing ointment for external use, in pharmacy, for cosmetics; but especially in the manufacture of nitro-glycerine and in the colour industry, and as an antifreeze. (Cf. J. Ind. 1928, 1073.)

Behaviour.—1. With alkalis and other metallic hydroxides it forms **alcoholates**, which are readily decomposed again into their components.

2. As a trihydric alcohol the hydrogen atoms of the OH groups can be replaced by alkyl radicals yielding **ethers**, *e.g.* **mono-ethylin,** $C_3H_5(OH)_2(OC_2H_5)$, and **triethylin,** $C_3H_5(OC_2H_5)_3$, liquids which boil without decomposition.

3. As an alcohol it forms the most various **esters**: thus, with sulphuric acid, the easily saponifiable **glyceryl-sulphuric acid,** $C_3H_5(OH)_2(O \cdot SO_3H)$; with phosphoric acid, **glyceryl-phosphoric acid,** $C_3H_5(OH)_2(O \cdot PO_3H_2)$; with nitric acid, **glyceryl trinitrate,** $C_3H_5(O \cdot NO_2)_3$; with hydrochloric acid the **chlorhydrins**; and with the higher fatty acids the fats. For its behaviour with hydriodic acid, or iodine and phosphorus, see p. 63.

4. It yields compounds of a mercaptan or aminic character by exchange of OH for SH or NH_2.

5. When distilled with dehydrating agents, *e.g.* phosphorus pentoxide, or, better, anhydrous potassium hydrogen sulphate, two molecules of water are eliminated from each molecule of glycerol, and acrolein (p. 137) is formed. By the indirect separation of one mol. H_2O, **glycide alcohol,** $C_3H_6O_2$, is obtained.

6. Oxidizing agents convert it, according to circumstances, either into **glyceric,** $OH \cdot CH_2 \cdot CH(OH) \cdot CO_2H$, **tartronic,** $CO_2H \cdot CH(OH) \cdot CO_2H$, or **mesoxalic acid,** $CO_2H \cdot CO \cdot CO_2H$, or acids with a smaller number of carbon atoms. The formation of the three above-mentioned acids indicates that glycerol molecule must be built up of two primary and one secondary alcoholic groups, as represented in the formula already given. Halogens oxidize and do not substitute.

7. It yields normal butyl alcohol, caproic acid, and butyric acid by certain fermentations. (Cf. B. 16, 884.)

8. It is used in the preparation of allyl alcohol (p. 85),

acrolein (p. 137), allyl iodide (p. 68), isopropyl iodide (p. 63), and formic acid (p. 154).

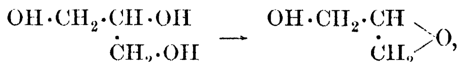
DERIVATIVES

Chlorhydrins (hydrochloric esters). **Mono-** and **dichlorhydrins** are formed by the action of hydrochloric acid on glycerol, and **trichlorhydrin** by the action of phosphorus pentachloride on the mono- or di-compounds. Each of the two first-named exists in two isomeric modifications.

α-**Monochlorhydrin,** 3-*Chloro-propane*-1:2-*diol*, $CH_2(OH)\cdot CH(OH)\cdot CH_2Cl$, is formed from epichlorhydrin, $C_3H_5O\cdot Cl$, (see below), and water; α-**dichlorhydrin,** 1:3-*dichloro-propane-2-ol*, $CH_2Cl\cdot CH(OH)\cdot CH_2Cl$, from epichlorhydrin and HCl; β-**monochlorhydrin,** $CH_2(OH)\cdot CHCl\cdot CH_2(OH)$, and β-**dichlorhydrin,** $CH_2Cl\cdot CHCl\cdot CH_2\cdot OH$, by the addition of hypochlorous acid to allyl alcohol or to allyl chloride.

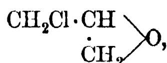
The chlorhydrins are liquids sparingly soluble in water, and readily soluble in alcohol and ether. Their boiling-points are much below that of glycerol.

Glycide Compounds.—By the elimination of water from glycerol a compound is obtained which unites within itself the properties of ethylene oxide and of a monohydric alcohol, viz. **glycide alcohol.** It is a 1 : 2·cyclic oxide or ether and



is isomeric with propionic acid.

It may be prepared by the abstraction of HCl from α-monochlorhydrin by means of baryta, just as ethylene chlorhydrin yields ethylene oxide. It is a colourless liquid, boiling at 162°, and miscible with water, alcohol, and ether. It combines with H_2O, yielding glycerol, and with HCl yielding the chlorhydrin, and, as an alcohol, forms esters (glycide esters), &c. Its hydrochloric ester is **epichlorhydrin,**



isomeric with chlor-acetone and propionyl chloride, a mobile liquid of chloroform odour, boiling at 117°, which is formed by the elimination of HCl from either of the dichlorhydrins. Like ethylene oxide it is capable of combining with H_2O, HCl, &c.

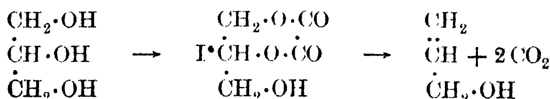
Esters of Nitric Acid.—Mononitrin, $C_3H_5(OH)_2(O\cdot NO_2)$,

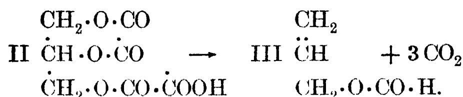
and **trinitrin** or **nitro-glycerine,** $C_3H_5(O\cdot NO_2)_3$, are known. The latter is prepared by treating glycerol with a cold mixture of concentrated nitric and sulphuric acids (B. 1899, **32,** 1444). It is a colourless oil, insoluble in water, poisonous, and of a sweet, burning, aromatic taste. Sp. gr. 1·6. M.-pt. about 11°–12°. It solidifies on cooling, and exists in two physical crystalline isomerides (*Hepworth*, J. C. S. 1919, **115,** 840). It burns without explosion, but explodes with terrible violence when quickly heated or when struck (*Nobel's* explosive oil). When mixed with kieselguhr in the proportion of three parts to one it forms **dynamite** (*Nobel*, 1867), which is exploded by fulminate of mercury with frightful force. It is hydrolysed by alkalis and by ammonium sulphide, yielding glycerol and nitric acid, and hence its constitution as a nitrate, $C_3H_5(O\cdot NO_2)_3$, and not a nitro-derivative, *e.g.* $C_3H_2(NO_2)_3(OH)_3$.

The natural glycerides are mostly normal esters, *e.g.* **glyceryl tripalmitate, tripalmitin,** $C_3H_5(O\cdot CO\cdot C_{15}H_{31})_3$, **tristearin,** &c. (see p. 164, *et seq.*). These esters can also be obtained artificially, as can also the mono- and dihydric esters, *e.g.* **monopalmitin,** $(OH)_2C_3H_5\cdot O\cdot CO\cdot C_{15}H_{31})$, and **dipalmatin,** $OH\cdot C_3H_5(O\cdot CO\cdot C_{15}H_{31})_2$, and mixed glycerides (p. 166).

Most are wax-like solids, and, on hydrolysis, yield as ultimate products glycerol and the fatty acid. With the normal esters this hydrolysis occurs in stages yielding the monohydroxy ester, then the dihydroxy, and finally glycerol.

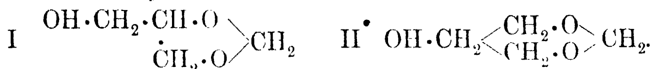
Glyceryl oxalates play an important part in the conversion of oxalic acid into formic acid and of glycerol into allyl alcohol. The first of these reactions has already been described (p. 154). The formation of allyl alcohol probably proceeds in the following stages. (*Chattaway*, J. C. S. 1914, **105,** 153.) By the action of oxalic acid upon glycerol a certain amount of the neutral oxalate (dioxalin) I is formed in addition to the acid oxalate (p. 154 and 85). The neutral oxalate decomposes at the higher temperature into carbon dioxide and allyl alcohol. Some of the glycerol may form the trioxalate (trioxalin) II, which then decomposes into carbon dioxide and allyl formate III, which is always formed as a by-product.





The glyceryl esters of phosphoric acid, H_3PO_4, are compounds of interest as they are related to natural products such as the lecithins (Chap. XLIII). Both α and β monophosphates, viz. $OH\cdot CH_2\cdot CH(OH)\cdot CH_2\cdot O\cdot PO(OH)_2$ and $(OH\cdot CH_2)_2CH\cdot O\cdot PO(OH)_2$, have been prepared, the former from α-monochlorhydrin and trisodium phosphate and the latter from phosphoryl chloride, and the α-dichlorhydrin and subsequent hydrolysis (*King* and *Pyman*, *ibid.* 1238; *Bailly*, C. R. 1915, **161**, 677. For methods of discrimination between α- and β-glycerophosphates, cf. *Grimbert* and *Bailly*, C. R. 1915, **160**, 207.)

Glycerol condenses with aldehydes and ketones in the presence of hydrogen chloride, giving both 5 and 6 membered cyclic acetals, *e.g.* I and II with formalin:



The structure of the compounds was proved by final conversion into β- and α-methyl ethers of glycerol respectively, after separation by means of their benzoyl derivatives (J. C. S. 1915, 337; *Hibbert* and others J. A. C. S. 1928, 2238, 3120, 3376; 1929, 302, 3644; *Fairbourne*, J. C. S. 1929, 2234). Mono alkyl ethers of glycerol occur in fish oils, *e.g. batyl alcohol* and the unsaturated *selachyl alcohol.*

C. Tetra-, Penta-, and Hexahydric Alcohols

These alcohols can react respectively with 4, 5, or 6 molecules of a monobasic acid to form neutral esters, and consequently 4, 5, or 6 alcoholic hydroxyls are to be assumed as present in their molecules.

The number of hydroxyls present in an alcohol is usually determined from the number of acetyl groups present in the ester which is formed when the alcohol is heated with acetic anhydride and anhydrous sodium acetate, thus:—



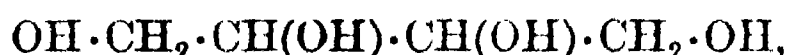
$$C_6H_8(OH)_6 + 6(CH_3\cdot CO)_2O = C_6H_8(O\cdot CO\cdot CH_3)_6 + 6CH_3\cdot CO_2H.$$

The acetyl derivative is then hydrolysed with alcoholic potash and the amount of potash used up determined by titration, or is distilled with benzene sulphonic acid and the distillate titrated.

The ester of any alcohol in question may also be prepared by the aid of an acid containing halogen, bromo-benzoic acid being especially suitable for this; and from the percentage of bromine found in the ester, the number of acid radicals which have entered the molecule, *i.e.* the number of hydroxyls, can be deduced.

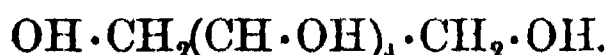
The polyhydric alcohols are solid crystalline compounds of sweet taste. Many occur as natural products, and they may be obtained by the reduction of the corresponding hydroxy aldehydes, hydroxy ketones, or hydroxy monobasic acids (mannonic acid, &c.) by sodium amalgam. (*E. Fischer*, B. **22**, 2204.) Conversely, cautious oxidation by bromine water transforms them first into sugars (hydroxy aldehydes), and then into the corresponding acids. As a rule they cannot be volatilized without decomposition. Their derivatives are exactly analogous to those of glycol and glycerol.

Their *constitution* follows from the generalization already repeatedly referred to, viz. that not more than one hydroxyl group can be attached to the same carbon atom without the immediate separation of water, so that a tetrahydric alcohol must contain at least 4, and a hexahydric alcohol at least 6, atoms of carbon. The tetrahydric alcohol erythritol, $C_4H_6(OH)_4$, has thus the formula:



$$OH \cdot CH_2 \cdot CH(OH) \cdot CH(OH) \cdot CH_2 \cdot OH,$$

and mannitol, the simplest of the hexahydric alcohols, $C_6H_8(OH)_6$, the formula:



$$OH \cdot CH_2(CH \cdot OH)_4 \cdot CH_2 \cdot OH.$$

All the common polyhydric alcohols have a normal carbon chain, as on reduction with hydriodic acid they yield normal secondary iodides, *e.g.* erythritol yields 2-iodo-butane, $CH_3 \cdot CHI \cdot CH_2 \cdot CH_3$.

1. **Tetrahydric Alcohols.—Ortho-carbonic ether,** $C(OC_2H_5)_4$, is to be regarded as the ether of the hypothetical alcohol, $C(OH)_4$, which may be looked upon as the hydrate of carbonic acid, but is itself incapable of existence. It is a liquid of ethereal odour, boiling at 159°.

Erythritol (*Butane-tetrol*) occurs in the free state in *Protococcus vulgaris*, and combined with orsellinic acid as an ester (erythrin), in many lichens and algæ. It forms large quadratic crystals, sparingly soluble in alcohol and insoluble in ether. M.-pt. 112°; b.-pt. about 300°.

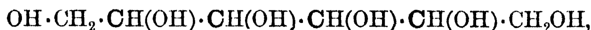
2. **Pentahydric Alcohols, Arabitol,** $OH \cdot CH_2 \cdot (CH \cdot OH)_3 \cdot$

$CH_2 \cdot OH$ (from arabinose by reduction). **Xylitol**, by the reduction of xylose, is stereo-isomeric; and **rhamnitol**, $OH \cdot CH_2 \cdot (CH \cdot OH)_4 \cdot CH_3$, m.-pt. 121°, from rhamnose, is homologous.

3. **Hexahydric Alcohols.—Mannitol**, $OH \cdot CH_2 \cdot (CH \cdot OH)_4 \cdot CH_2 \cdot OH$ (*Proust*, 1800), is found in many plants, for instance in the larch, in *Viburnum Opulus*, in celery, in the leaves of *Syringa vulgaris*, in sugar-cane, in *Agaricus integer* (of the dry substance of which it forms 20 per cent), in rye bread, and especially in the manna ash, *Fraxinus ornus*, the dried juice of which constitutes manna. It can be prepared from grape-sugar, or still better from fruit sugar, from which it only differs in composition by containing two atoms of hydrogen more in the molecule, by reduction with sodium amalgam.

It crystallizes in fine needles or rhombic prisms, and is readily soluble in cold water and boiling alcohol. It is dextro-rotatory, but a lævo-rotatory and an inactive modification are also known. (See Mannonic Acid.) M.-pt. 166°. When heated it is converted into its anhydrides, **mannitan**, $C_6H_{12}O_5$, and **mannide**, $C_6H_{10}O_4$. Cautious oxidation converts mannitol into a mixture of mannose, $OH \cdot CH_2(CH \cdot OH)_4 \cdot CHO$, and fructose, $OH \cdot CH_2(CH \cdot OH)_3 \cdot CO \cdot CH_2 \cdot OH$. Nitric acid oxidizes it to saccharic acid, $CO_2H \cdot (CH \cdot OH)_4 \cdot CO_2H$; hydriodic reduces it to secondary hexyl iodide, $CH_3 \cdot CHI \cdot (CH_2)_3 \cdot CH_3$ (p. 62).

The molecule of mannitol contains 4 asymmetric carbon atoms, *e.g.*:



$$OH \cdot CH_2 \cdot CH(OH) \cdot CH(OH) \cdot CH(OH) \cdot CH(OH) \cdot CH_2OH,$$

and hence a number of stereo-isomerides are known, *e.g.* *d*-, *l*-, and *r*-mannitol, *d*-, *l*-, *r*-**sorbitol**, and **dulcitol**, which is optically inactive owing to the fact that its molecule is symmetrical in configuration. (Stereochemistry of Sugars, Chap. XIV, A.)

The sugars are closely related to the penta- and hexahydric alcohols, being the corresponding polyhydric aldehydes or ketones. The alcohols as a rule are not fermented by yeast, and do not reduce an alkaline cupric solution, dulcitol excepted.

OXIDATION PRODUCTS OF THE POLYHYDRIC ALCOHOLS

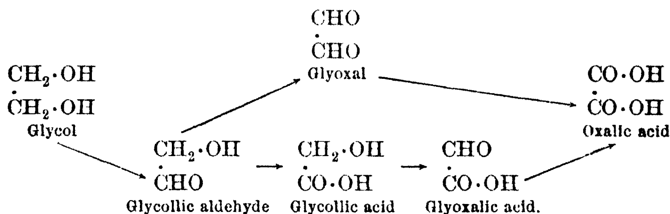
Just as the monohydric alcohols are oxidized to aldehydes, ketones, and acids, so the polyhydric alcohols pass, on oxidation, into aldehydes, ketones, and polybasic acids.

Further, by this oxidation of the polyhydric alcohols we obtain not only aldehydes, ketones, and acids, but also numerous compounds which possess a double chemical character in so far as they unite in themselves the properties of more than one of these classes of compounds. These are the **hydroxy aldehydes**, which are at the same time aldehyde and alcohol, the **hydroxy ketones**, at the same time ketone and alcohol, the **hydroxy acids, aldehyde acids, ketone acids**, and **ketone aldehydes**.

An aldehyde acid, for instance, is capable, as an acid, of forming salts, esters, and amides on the one hand; and on the other, as an aldehyde, it is able to reduce an ammoniacal silver solution, to combine with $NaHSO_3$, and to react with hydroxylamine, &c.

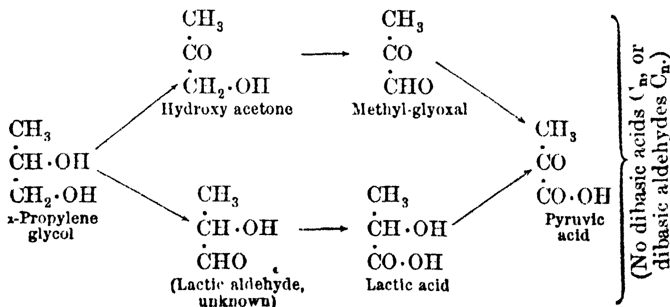
SUMMARY OF THE OXIDATION PRODUCTS

(*a*) Of the di-primary alcohols.



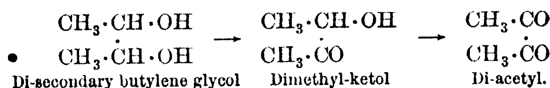
Possible products: Di-aldehydes, dibasic acids, hydroxy aldehydes, hydroxy acids, aldehyde acids.

(*b*) Of the hydroxy primary-secondary alcohols.



Possible products: hydroxy aldehydes, hydroxy ketones, ketone aldehydes, hydroxy acids, ketone acids.

(*c*) Of the di-secondary alcohols: hydroxy ketones, diketones. (No dibasic acids or alcohol acids, C_n.) *e.g.*:



(*d*) The tri- and polyhydric alcohols are capable of yielding numerous types of products upon oxidation, especially polyhydroxy ketones, polyhydroxy acids, keto-acids, and polybasic acids.

Of all these oxidation products, the most important, are the hydroxy acids, the polybasic acids, and the keto-acids. For the sake of convenience the hydroxy monobasic acids will be treated of first.

IX. HYDROXY MONOBASIC ACIDS AND COMPOUNDS RELATED TO THEM

A. Monohydroxy Fatty Acids

These compounds may be regarded as monohydroxy derivatives of the fatty acids, *e.g.* $OH \cdot CH_2 \cdot CO_2H$, hydroxy acetic acid, or glycollic acid, $OH \cdot CH_2 \cdot CH_2 \cdot CO_2H$, β-hydroxy propionic acid, or β-lactic acid, &c.

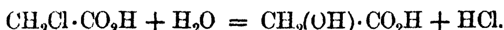
They combine within themselves the **properties of a monobasic acid and of an alcohol**, and are consequently capable of forming derivatives as alcohols, as acids, and as both together.

The lowest members of the series, which are the most important, are **glycollic acid** and **lactic acid**, both syrupy liquids which solidify to crystalline masses in the desiccator, and readily give up water to form anhydrides. They cannot be volatilized without decomposition; and are readily soluble in water, and for the most part also in alcohol and ether.

Formation.—1. By the regulated oxidation of the glycols. (See Summary, p. 212.)

2. From the fatty acids, through their monohaloid substitution products, the halogen of these being easily replaced by

hydroxyl, either by means of **moist oxide of silver** or **often by** prolonged boiling with water alone:



$$CH_2Cl\cdot CO_2H + H_2O = CH_2(OH)\cdot CO_2H + HCl.$$

This reaction is conditioned by the halogen having the α-position with respect to the carboxyl (cf. pp. 175 and 176).

For a reaction of these haloid-substitution products in a different direction, see β- and γ-hydroxy acids.

3. From the aldehydes and ketones containing 1 atom of carbon less, by the preparation of their hydrocyanic acid compounds, **cyanhydrins** (see pp. 133 and 142), and hydrolysis of the latter. Thus, from aldehyde is produced ethylidene cyanhydrin, and from this α-lactic acid:



$$CH_3\cdot CH(OH)(CN) + 2H_2O = CH_3\cdot CH(OH)\cdot CO_2H + NH_3.$$

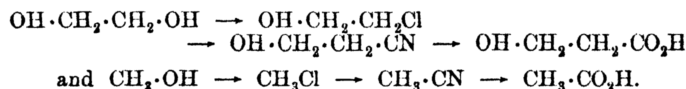
Since the aldehydes and ketones are easily obtained from the corresponding alcohols, this reaction furnishes a means of preparing the acids, $C_nH_{2n}(OH)(CO_2H)$, from the alcohols, $C_nH_{2n+1}(OH)$, *i.e.* of introducing carboxyl into the latter in place of hydrogen; this is a most important synthesis.

4. From the glycollic cyanhydrins by saponification, *e.g.* β-lactic acid from ethylene cyanhydrin:



$$OH\cdot CH_2\cdot CH_2\cdot CN + 2H_2O = OH\cdot CH_2\cdot CH_2\cdot CO_2H + NH_3.$$

As the cyanhydrins can be readily obtained from the glycols (p. 198), this formation of hydroxy acids represents an exchange of a hydroxyl of the glycol for carboxyl, and is analogous to the formation of acetic acid from methyl alcohol. Thus:—



$$OH\cdot CH_2\cdot CH_2\cdot OH \rightarrow OH\cdot CH_2\cdot CH_2Cl \rightarrow OH\cdot CH_2\cdot CH_2\cdot CN \rightarrow OH\cdot CH_2\cdot CH_2\cdot CO_2H$$

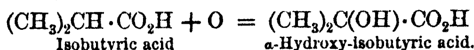
$$\text{and } CH_3\cdot OH \rightarrow CH_3Cl \rightarrow CH_3\cdot CN \rightarrow CH_3\cdot CO_2H.$$

5. By the reduction of aldehyde acids or ketonic acids, *e.g.* lactic from pyruvic acid (p. 233). This reaction corresponds with the formation of the alcohols from the aldehydes or ketones by reduction.

6. By the action of nitrous acid upon amino acids (see Glycocoll); a reaction analogous to the formation of alcohols from amines (p. 111).

7. Hydroxy acids of the fatty series containing an equal number of carbon atoms result by *direct oxidation*, if a CH

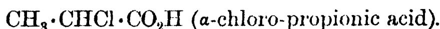
group, *i.e.* a "tertiary" hydrogen atom, is present in the original acid (*R. Meyer*, B. **11**, 1283; **12**, 2238):



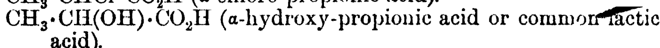
$$(CH_3)_2CH \cdot CO_2H + O = (CH_3)_2C(OH) \cdot CO_2H$$

Isobutyric acid — α-Hydroxy-isobutyric acid.

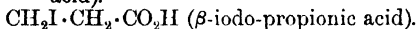
Constitution and Isomers.—As hydroxy compounds of the fatty acids, the acids of the foregoing series can exist in as many modifications as the monohalide fatty acids. Thus there is only one glycollic acid, corresponding with monochloracetic acid, but two lactic acids—corresponding with α- and β-chloropropionic acids—are possible, and both actually exist; they are designated as α- and β-hydroxy propionic acids:



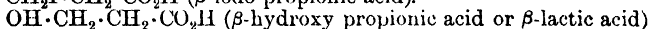
$CH_3 \cdot CHCl \cdot CO_2H$ (α-chloro-propionic acid).



$CH_3 \cdot CH(OH) \cdot CO_2H$ (α-hydroxy-propionic acid or common lactic acid).



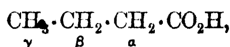
$CH_2I \cdot CH_2 \cdot CO_2H$ (β-iodo-propionic acid).



$OH \cdot CH_2 \cdot CH_2 \cdot CO_2H$ (β-hydroxy propionic acid or β-lactic acid)

From the two butyric acids can be theoretically derived:

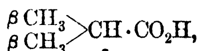
(*a*) From the normal acid:



$$\underset{\gamma}{CH_3} \cdot \underset{\beta}{CH_2} \cdot \underset{\alpha}{CH_2} \cdot CO_2H,$$

an α-, β-, and γ-hydroxy butyric acid.

(*b*) From isobutyric acid:



$$\begin{matrix}\beta\, CH_3 \\ \beta\, CH_3\end{matrix}\!\!>\underset{\alpha}{CH} \cdot CO_2H,$$

an α- and β-hydroxy isobutyric acid.

Systematic Nomenclature.—$OH \cdot CH_2 \cdot CH_2 \cdot CO_2H$, *Propane-3-ol-1-acid*; $(CH_3)_2 \cdot C(OH) \cdot CO_2H$, *2-Methyl-propane-2-ol-1-acid*; $OH \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CO_2H$, *Butane-4-ol-1-acid*, &c.

The constitution of these hydroxy acids can often be deduced from their methods of formation. Thus the preparation of common lactic acid from aldehyde, $CH_3 \cdot CHO$, according to method 3, shows that it contains the group $CH_3 \cdot CH:$, "ethylidene"; it is therefore termed "ethylidene lactic acid". On the other hand, the formation of β-hydroxy propionic acid from glycol cyanhydrin, according to 4, is a proof of its containing the group $\cdot CH_2 \cdot CH_2 \cdot$, "ethylene"; hence the name "ethylene lactic acid".

The constitution can also frequently be deduced from a study of their oxidation products; if they can be oxidized, for instance, to dibasic acids (which contain two carboxyls)

then they must contain a primary alcohol group, $\cdot CH_2 \cdot OH$, since only such a group yields a new carboxyl on oxidation. Ethylene lactic acid is therefore a "primary" alcohol acid. Its isomer, ethylidene lactic acid, is similarly a "secondary" alcohol acid, while α-hydroxy isobutyric acid is a "tertiary" alcohol acid, *i.e.* acid and tertiary alcohol at the same time.

Behaviour.—1. The double chemical character of the hydroxy acids will be dealt with more in detail under Glycollic Acid. As acids they form salts, esters, and amides; as alcohols they yield ethers, amines, &c. Of these derivatives the alcoholic amines of the acids, the so-called amino acids, are of especial interest. (See Glycocoll, p. 219.)

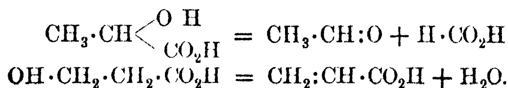
2. The hydroxy acids form different kinds of anhydrides, viz.: (*a*) as alcohols (see Di-glycollic Acid); (*b*) one molecule as alcohol forms with a second molecule as acid an ester, with elimination of H_2O (see Glycollic Anhydride); (*c*) operation *b* is repeated, the first molecule acting as acid, and the second as alcohol (see Glycolide); (*d*) one molecule loses H_2O, with formation of an "intramolecular" anhydride, a so-called *lactone* (see p. 225.)

3. For behaviour upon oxidation see p. 215, and also the individual compounds.

4. Just as the alcohols readily give up water, yielding olefines, so many of the hydroxy acids, especially the β-, can be transferred into unsaturated monobasic acids. (See Hydracrylic Acid, p. 221.)

5. When warmed with hydriodic acid, the hydroxy acids are reduced to the corresponding fatty acids, just as the alcohols are converted by this reagent into hydrocarbons.

6. When the α-hydroxy acids are warmed with dilute sulphuric acid, formic acid is produced together with the aldehyde or ketone which would give rise to the acid, according to method 3. The β-hydroxy acids, on the other hand, decompose into water and acids of the acrylic series. Thus:—



$$CH_3 \cdot CH \langle {OH \atop CO_2H} = CH_3 \cdot CH{:}O + H \cdot CO_2H$$

$$OH \cdot CH_2 \cdot CH_2 \cdot CO_2H = CH_2{:}CH \cdot CO_2H + H_2O.$$

The α-, β-, γ-, &c., hydroxy acids also differ from each other in the facility with which they form anhydrides. (See Lactones, p. 225.)

Glycollic Acid, *Hydroxy-acetic acid*, *Ethanolic acid*, $OH \cdot CH_2 \cdot CO_2H$ (*Strecker*, 1848), occurs in unripe grapes, in the leaves of the wild vine, &c.

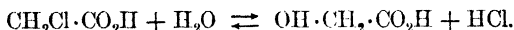
Formation.—1. By the oxidation of glycol with dilute HNO_3 (*Wurtz*).

2. Together with glyoxal and glyoxylic acid, by the oxidation of alcohol with dilute HNO_3.

3. By the reduction of oxalic acid with $Zn + H_2SO_4$.

4. From formaldehyde synthetically, according to method 3, p. 214.

5. It is usually prepared by boiling chloro-acetic acid with water in the presence of marble, the marble serving to neutralize the HCl formed in the reaction (A. **200**, 76):



$$CH_2Cl \cdot CO_2H + H_2O \rightleftarrows OH \cdot CH_2 \cdot CO_2H + HCl.$$

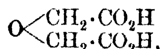
Properties.—It forms colourless needles or plates, is readily soluble in water, alcohol, and ether, and melts at 80°. Nitric acid oxidizes it to oxalic acid. The alkaline salts are hygroscopic, the calcium salt and the magnificent blue copper salt are sparingly soluble in water. $K = 0{\cdot}0152$.

Derivatives.—(See table, p. 218.) As an acid, glycollic acid forms salts, esters—*e.g.* **ethyl glycollate**—a chloride, **glycollyl chloride**, and **glycollamide**, all of which are readily hydrolysed, some of them even on warming with water. All those derivatives still retain their alcoholic character. If, on the other hand, glycollic acid forms derivatives as an alcohol, the properties of the alcoholic derivatives in question are combined with those of an acid, since the hydroxyl of the alcoholic group, $\cdot CH_2 \cdot OH$, enters into reaction, while the carboxyl group remains unchanged. These derivatives are either ethers, such as **ethyl-glycollic acid** (see table), or *e.g.* amines, such as **glycocoll**, and, as alcoholic derivatives, they are not readily hydrolysed; or they are esters of glycollic acid, as alcohol, *e.g.* **acetyl-glycollic acid**, $CH_2(O \cdot CO \cdot CH_3) \cdot CO_2H$, or **monochloracetic acid**, $CH_2Cl \cdot CO_2H$ (the hydrochloric ester of glycollic acid), and then they are of course saponifiable. These latter compounds still retain their acid character, and therefore form, on their part, esters, chlorides, and amides, which are also readily hydrolysed. The following table gives a summary of the more important derivatives of glycollic acid:—

Acid Derivatives	Alcoholic Derivatives.	Mixed Derivatives.
$HO \cdot CH_2 \cdot CO \cdot ONa$ Sodium glycollate.		$NaO \cdot CH_2 \cdot CO \cdot ONa$ Di-sodium glycollate. Hygroscopic; decomp. by H_2O into Na salt and NaOH.
$HO \cdot CH_2 \cdot CO \cdot OC_2H_5$ Ethyl glycollate. Liquid, b.-pt. 160°.	$OC_2H_5 \cdot CH_2 \cdot CO \cdot OH$ Ethyl-glycollic acid. Liquid, b.-pt. 206°.	$C_2H_5 \cdot O \cdot CH_2 \cdot CO \cdot OC_2H_5$ Ethylic ethyl-glycollate. Liquid, b.-pt. 152°.
$HO \cdot CH_2 \cdot CO \cdot Cl$ Glycollyl chloride. Oil; decomposes on volatilizing.	$CH_2Cl \cdot CO \cdot OH$ Monochloracetic acid.	$CH_2Cl \cdot COCl$ Monochloracetyl chloride. Liquid, b.-pt. 120°, of suffocating odour.
$HO \cdot CH_2 \cdot CO \cdot NH_2$ Glycollamide. Crys. M.-pt. 120°; does not form salts with bases.	$NH_2 \cdot CH_2 \cdot CO \cdot OH$ Glycocoll. Crys. M.-pt. 236°. Forms salts with acids and bases.	$NH_2 \cdot CH_2 \cdot CO \cdot NH_2$ Glycocollamide. Crys.

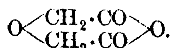
It is easy to see that the corresponding derivatives of the first and second vertical rows are always isomeric.

Anhydrides of Glycollic Acid.—1. Glycollic acid can yield different types of anhydrides: (1) the elimination of one mol. of water from the alcoholic hydroxyls of two molecules of the acid produces **diglycollic acid,**



which is obtained by boiling monochloracetic acid with lime. It forms large rhombic prisms, is a dibasic acid, and, as an ether, is not saponified when boiled with alkalis, but is decomposed when heated with concentrated hydrochloric acid to 120°.

2. Diglycollic acid loses water when heated, yielding the **diglycollic anhydride,**



3. **Glycollic anhydride,** $OH \cdot CH_2 \cdot CO \cdot O \cdot CH_2 \cdot CO_2H$, is an ester, which is formed when glycollic acid is heated at 100°. It becomes hydrated again when boiled with water, and may be regarded as an ester derived from glycollic acid acting as an alcohol and as an acid.

4. **Glycolide**, $\begin{matrix} CH_2\cdot O\cdot CO \\ \cdot \quad\quad \cdot \\ CO\cdot O\cdot CH_2 \end{matrix}$, is also an ester anhydride, and is isomeric with 2 (and with fumaric acid). It is formed when sodium bromo-acetate is distilled in a vacuum. Lustrous plates; m.-pt. 87°. It becomes hydrated again when boiled with water.

Glycocoll (*Amino-ethane acid*), *glycine*, *amino-acetic acid*, $NH_2\cdot CH_2\cdot CO_2H$ (*Braconnot*, 1820). This is the simplest representative of the important class of amino acids, so called because they are derived from the fatty acids by the exchange of a hydrogen atom of the hydrocarbon radical for an amino group, *e.g.* $CH_3\cdot CO_2H$, acetic acid; $CH_2(NH_2)\cdot CO_2H$, amino-acetic acid.

Formation.—1. By the action of concentrated ammonia upon monochloracetic acid (*Heintz*, A. **122**, 261; *Kraut*, A. **266**, 292):



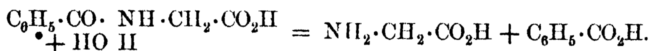
$$CH_2Cl\cdot CO_2H + 2NH_3 = NH_2\cdot CH_2\cdot CO_2H + NH_4Cl$$

(cf. also B. **23**, Ref. 654). Di- and triglycollamic acids, $NH(CH_2\cdot CO_2H)_2$ and $N(CH_2\cdot CO_2H)_3$, are produced at the same time.

α-Chloropropionic acid in like manner yields alanine with ammonia (see Lactic Acid). The method is a general one for the production of amino acids.

2. By boiling glue with alkalis or acids.

3. Together with benzoic acid, by decomposing hippuric acid, *i.e.* benzoyl-glycocoll, with concentrated hydrochloric acid:



$$\begin{matrix} C_6H_5\cdot CO\cdot\ NH\cdot CH_2\cdot CO_2H \\ +\ HO\ H \end{matrix} = NH_2\cdot CH_2\cdot CO_2H + C_6H_5\cdot CO_2H.$$

Properties.—Glycocoll forms large colourless rhombic prisms, readily soluble in water, but insoluble in absolute alcohol and ether. It has a sweet taste, hence the name "glue sugar" or glycocoll (γλυκύς, sweet, κόλλα, glue). It melts and decomposes at 236°. Glycocoll, like all the amino acids, possesses the properties of both an amine and an acid. It therefore forms salts with acids as well as with bases, *e.g.* glycocoll **hydrochloride**, $C_2H_5NO_2\cdot HCl$, which crystallizes in prisms, and the characteristic copper salt, **copper glycocoll**, $(C_2H_4NO_2)_2Cu + H_2O$, which crystallizes in blue needles, the latter being obtained by dissolving cupric oxide in a solution of glycocoll. Most of the other amino acids also form characteristic copper salts of this nature, which serve for their separation. Glycocoll

also yields compounds with salts, and, as an acid, forms an ethyl ester, an amide, &c. (see table, p. 218). When heated with BaO it is decomposed into methyl-amine and CO_2, while nitrous acid converts it into glycollic acid (the normal reaction of the primary amines). With ferric chloride it produces an intense red, and with copper salts a deep-blue coloration.

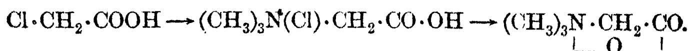
Ethyl amino-acetate (b.-pt. 43°/11 mm.) and nitrous acid yield the interesting **ethyl diazo-acetate**, $\overset{N}{\underset{N}{\vdots}}\!\!>CH\cdot CO\cdot OC_2H_5$, from which hydrazine, $NH_2\cdot NH_2$, and its hydrate were first prepared; and from the latter the remarkable compound, hydrazoic acid, N_3H (*Curtius*; see also Di and Triazo Derivatives, Chap. LI.).

Constitution (see B. **16**, 2650).—Free glycocoll may possibly be an intramolecular salt, corresponding with the formula $CH_2<\begin{smallmatrix}NH_3\\CO\cdot O\end{smallmatrix}>$ (see Taurine, p. 204, and Betaine below). The absence of a free CO_2H group in many amino-acids is indicated by the fact that diazo-methane is without action on many of them. (Z. physiol., 1914, **92**, 149; *Noyes* and *Potter*, J., A. C. S. 1915, **37**, 189.)

Alkyl and Acyl Derivatives of Glycocoll:

Methyl-glycocoll or Sarcosine,	Trimethyl-glycocoll or Betaïne,	Acetyl-glycocoll or Aceturic Acid,
$CH_2\cdot NHCH_3$ / $CO\cdot OH$	$CH_2\cdot N(CH_3)_3$ / $CO\cdot O$ (ring)	$CH_2\cdot NH\cdot CO\cdot CH_3$ / $CO\cdot OH$.

Many of these alkyl derivatives occur as such in natural products, or may be obtained by the decomposition of certain natural compounds. Sarcosine is obtained by the decomposition of the complex natural substances creatine or caffeine. Betaïne occurs in beet-root, and is present in large quantities in the molasses from beet-root sugar (B. 1912, **45**, 2248). It crystallizes with 1 H_2O, which it readily gives up on heating. When heated at 293° betaine is transformed into the isomeric methyl ester of dimethylaminoacetic acid, $NMe_2\cdot CH_2\cdot CO\cdot OMe$; at higher temperatures it yields trimethylamine. It has been synthesized by the action of trimethylamine on monochloracetic acid (B. 1902, **35**, 603):



$$Cl\cdot CH_2\cdot COOH \rightarrow (CH_3)_3N(Cl)\cdot CH_2\cdot CO\cdot OH \rightarrow (CH_3)_3N\cdot CH_2\cdot CO\,(\text{—O—})$$

The substituted betaïnes with alkyl in the CH_2 group readily yield trimethylamine and $\alpha\beta$-unsaturated acids when heated, and such acids are often found in nature with tertiary amines. For dipolar structure of betaïnes see *Pfeiffer*, B. 1922, 1762.

Lactic Acids (*Hydroxy-propionic acids*). (*Wislicenus*, A. **128**, 1; **166**, 3; **167**, 304, 346.)—As has been already mentioned, two isomeric lactic acids are theoretically possible, viz. α- and β-hydroxy-propionic acids, and both of these are known.

The minute investigation of the different lactic acids has been of very great importance for the development of chemical theory; they were formerly held to be dibasic, and the recognition of their hydroxy-monobasic nature has materially contributed to the acceptation of the theory of atomic linking.

The molecule of α-hydroxy-propionic acid contains an asymmetric carbon atom, $CH_3 \cdot \mathbf{C}H\begin{smallmatrix} OH \\ CO_2H \end{smallmatrix}$, and hence should exhibit exactly the same kind of isomerism as was met with in the case of active valeric acid (p. 160).

In reality two optically active α-lactic acids are known, one of which is dextro (*d*), and the other lævo (*l*) rotatory. These two acids are identical in all their properties, with the exception of optical activity. A mixture (or compound) of the two in equal quantities is optically inactive, and is known as inactive (*dl*) or racemic (*r*) lactic acid.

The molecule of β-hydroxy-propionic acid does not contain an asymmetric carbon atom, and hence exists in only one modification, which is optically inactive.

Modes of Formation.	Fermentation Lactic Acid.	Ethylene-lactic Acid.
1. By the regulated oxidation of	α-Propylene glycol, $CH_3 \cdot CH(OH) \cdot CH_2OH$.	β-Propylene glycol, $OH \cdot CH_2 \cdot CH_2 \cdot CH_2OH$
2. By the exchange of halogen for hydroxyl in	α-Chloro-propionic acid, $CH_3 \cdot CHCl \cdot CO \cdot OH$.	β-Iodo-propionic acid, $CH_2I \cdot CH_2 \cdot CO \cdot OH$.
3. By hydrolysis of	Aldehyde-cyanhydrin, $CH_3 \cdot CH(OH) \cdot CN$.	Ethylene-cyanhydrin, $OH \cdot CH_2 \cdot CH_2 \cdot CN$.
4. By action of nitrous acid upon	Alanine, $CH_3 \cdot CH(NH_2) \cdot CO \cdot OH$.	
5. By the reduction of	Pyro-racemic acid, $CH_3 \cdot CO \cdot CO \cdot OH$.	
6. By the lactic fermentation of sugar, etc.		

1. **dl-Ethylidene-lactic Acid** (*Propane-2-ol-1-acid*), *ordinary fermentation lactic acid*, $CH_3 \cdot CH \cdot (OH) \cdot CO_2H$. Discovered by *Scheele*, and recognized as hydroxy-propionic acid by *Kolbe*. Occurs in opium, sauerkraut, and in the gastric juice.

Preparation.—This depends upon the so-called **lactic fermentation** of sugars, *e.g.* milk, cane- and grape-sugars, and of substances related to them, such as gum and starch; it is induced by certain species of bacteria commonly spoken of as the *lactic bacilli*. The fermentation proceeds best at a temperature of 34°–35° in a nearly neutral solution, this last condition being attained by the addition of chalk or zinc-white to the fermenting mixture. The free acid can then be liberated from the lactate of zinc by sulphuretted hydrogen. When a non-homogeneous ferment (*e.g.* decaying cheese) is used, the lactic acid at first produced is readily transformed by other organisms into butyric acid (p. 158).

Lactic acid is also produced in large quantity by heating grape- or cane-sugar with caustic-potash solution of a certain degree of concentration (B. **15**, 136). The relations of lactic acid to the sugar varieties appear, at a superficial glance, to be very simple; thus grape-sugar, $C_6H_{12}O_6$, and lactic acid, $C_3H_6O_3$, are polymers.

Lastly, the inactive acid is produced by mixing equal quantities of the two active modifications. In syntheses the latter are formed in equal amounts, and hence the inactive acid is obtained.

Properties.—When its solution is evaporated in a desiccator, a thick, non-crystallizing and hygroscopic syrup is obtained, which is miscible with water, alcohol, and ether, and which gradually loses water, yielding the solid lactic anhydride, $C_6H_{10}O_5$, before all the water of solution has been got rid of. To obtain the pure acid it is necessary to distil under very low pressures, when a crystalline solid melting at 18° is obtained. $K = 0{\cdot}0138$. When heated, it is partially converted into the anhydride, lactide, $C_6H_8O_4$, and partially into aldehyde, CO, and H_2O. Similarly it decomposes into aldehyde and formic acid when heated with dilute sulphuric acid to 130°, concentrated sulphuric giving rise to carbon monoxide instead of formic acid:



$$CH_3 \cdot CH(OH) \cdot CO_2H = CH_3 \cdot CHO + HCO_2H.$$

When oxidized, it yields acetic and carbonic acids; hydrobromic acid converts it into α-bromo-propionic acid, and boiling hydriodic acid into propionic acid itself.

The inactive acid is split up into the two active modifications by the crystallization of the strychnine salts (*Purdie* and *Walker*, J. C. S. 1892, 754); further, when green mould, *Penicillium glaucum*, is sown in a solution of the ammonium salt of the inactive acid, the lævo-acid is assimilated more rapidly than the dextro-, and the solution thus becomes optically active (*Linossier*, B. 1891, **24**, 660). A very simple resolution has been accomplished by *Purdie* (J. C. S. 1893, 1143) by crystallizing the zinc ammonium salt, $ZnC_6H_{10}O_6$, $NH_4C_8H_5O_3$, $2H_2O$. (Cf. Resolution of Racemic Acid.)

A number of well-defined salts are known, *e.g.* **Calcium lactate**, $(C_8H_5O_8)_2Ca + 5H_2O$; **zinc lactate**, $(C_3H_5O_3)_2Zn + 3H_2O$; **ferrous lactate**, $(C_3H_5O_3)_2Fe + 3H_2O$. When sodium lactate is heated with sodium, **di-sodium lactate**, $CH_3 \cdot CH(ONa) \cdot CO_2Na$, which is at the same time a salt and an alcoholate, is formed.

The *derivatives* of lactic acid are derivatives of it either as acid or as alcohol, and are perfectly analogous to those of glycollic acid (see table, p. 218). Thus **ethyl-lactic acid**, α-ethoxy-propionic acid, $CH_3 \cdot CH(OC_2H_5) \cdot CO_2H$, a thick acid liquid which boils almost without decomposition, corresponds with ethyl-glycollic acid; **ethyl lactate**, which can be distilled without decomposition, with ethyl glycollate; **lactamide**, $CH_3 \cdot CH(OH) \cdot CO \cdot NH_2$, with glycollamide; and **alanine**, $CH_3 \cdot CH(NH_2) \cdot CO \cdot OH$, with glycocoll.

By the action of PCl_5, **lactyl chloride**, $CH_3 \cdot CHCl \cdot CO \cdot Cl$ (p. 177), is formed; as the chloride of α-chloro-propionic acid it is decomposed by water, yielding the latter acid and HCl.

The following anhydrides of lactic acid are known:—

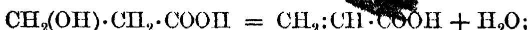
(1) **Lactylic acid** or **Lactic anhydride**, $C_6H_{10}O_5$, which is analogous to glycollic anhydride, and forms a yellow amorphous mass. (2) **Lactide**, $C_6H_8O_4$, analogous to glycolide (plates melting at 125°). (3) **Dilactic acid**, $C_6H_{10}O_5$, the alcoholic anhydride, analogous to diglycollic acid.

2. **d-Ethylidene-lactic acid**, *Sarco-lactic acid*, *para-lactic acid* (*Liebig*). This occurs in the juice of flesh, and is therefore to be found in Liebig's extract of meat. It results from certain fermentations. Its chemical properties are exactly similar to those of ordinary lactic acid; thus it readily yields lactide or aldehyde. Its salts differ to some extent, however, from those of the latter; thus, the **zinc salt**, $+ 2H_2O$, is much more easily soluble, and the **calcium salt** $+ 4H_2O$, much more sparingly soluble than the corresponding common lactates. Such differ-

ences are usually met with between *d*- and *l*-compounds on the one hand, and their *r*-isomeride on the other.

3. l-**Ethylidene-lactic acid** is obtained from the fermentation of cane-sugar by means of the *l-lactic bacillus.* Its salts correspond exactly with the salts of *d*-lactic acid. They have the same formulæ, same solubilities, &c.

4. **Ethylene-lactic acid** (*Propane-3-ol-1-acid*), *hydracrylic acid* (*Wislicenus*, A. **128**, 1), forms a syrupy mass. It differs from lactic acid (*a*) by its behaviour upon oxidation, yielding carbonic and oxalic acids, and not acetic; (*b*) by not yielding an anhydride when heated, but by breaking up into water and acrylic acid, hence the name hydracrylic acid:



$$CH_2(OH)\cdot CH_2\cdot COOH = CH_2{:}CH\cdot COOH + H_2O;$$

(*c*) in solubility, and in the amount of water of crystallization of its salts (*e.g.* zinc salt, $+ 4H_2O$, very readily soluble in water; calcium salt, $+ 2H_2O$). It is not so strong an acid as α-lactic acid. K = 0·00311.

It may be synthesised from ethylene by means of the following series of reactions: (*a*) the addition of hypochlorous acid, (*b*) conversion of the chlorhydrin into the corresponding nitrile, and (*c*) hydrolysis, *e.g.*:



$$CH_2{:}CH_2 \rightarrow OH\cdot CH_2\cdot CH_2Cl \rightarrow OH\cdot CH_2\cdot CH_2\cdot CN \rightarrow OH\cdot CH_2\cdot CH_2\cdot CO_2H.$$

Hydroxy-caproic Acids. **Leucine** or **α-Amino-caproic acid,** $CH_3\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH(NH_2)\cdot CO_2H$, is a derivative of α-hydroxy-caproic. It forms glistening plates, and, like other amino acids, is closely related to albumen. It is found in old cheese, also abundantly in the animal organism in the gastric gland, and in the shoots of the vetch and gourd, &c. It forms, along with tyrosine, a constant product of the digestion of albumen in the small intestine and of the decay of albuminous substances, and is formed when the latter are boiled with alkalis or acids. It has also been prepared synthetically. It closely resembles glycocoll, and forms a characteristic sparingly soluble blue copper salt. Leucine is dextro-rotatory. A lævo- and an inactive modification are also known (B. **24**, 669).

Le Sueur (J. C. S. 1904, 827; 1905, 1888) has prepared several hydroxy derivatives of the higher fatty acids, *e.g.* α-hydroxy margaric and α-hydroxy-stearic acids, and has found that a good yield (35–60 per cent) of an aldehyde can be obtained when the acid is heated to 240–250°. The molecule of the

aldehyde so obtained contains a carbon atom less than the molecule of the hydroxy acid, and water, formic acid, carbon monoxide, and a lactide are obtained as by-products.

LACTONES

All hydroxy acids tend to lose water under certain conditions, yielding anhydro-compounds.

The manner in which this water is eliminated is very different in the various types of hydroxy acids.

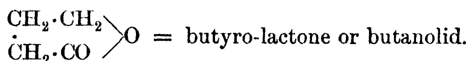
1. In the case of the α-hydroxy acids, 1 or 2 mols. of water are usually eliminated from 2 molecules of the acid, yielding compounds of the type of diglycollic acid, glycollic anhydride, &c.

2. In β-hydroxy acids 1 molecule of water is usually eliminated from 1 molecule of the acid, and an α-β-unsaturated acid is formed, *e.g.*:



$$CH_3 \cdot CH(OH) \cdot CH_2 \cdot CO_2H \longrightarrow CH_3 \cdot CH:CH \cdot CO_2H \text{ (crotonic acid).}$$

3. In the case of γ-hydroxy acids, *e.g.* γ-hydroxy-butyric acid, $OH \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CO_2H$, 1 molecule of water is eliminated from 1 molecule of the acid, and an inner anhydride or **lactone** is formed,



$$\begin{matrix} CH_2 \cdot CH_2 \\ CH_2 \cdot CO \end{matrix} \rangle O = \text{butyro-lactone or butanolid.}$$

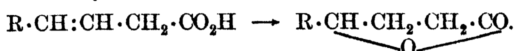
The formation of such a lactone is characteristic of γ-hydroxy acids. Many of these acids are so unstable in the free state, that when mineral acid is added to their salts the lactones and not the free acids are obtained.

The "γ-lactones" are for the most part neutral liquids of faint aromatic odour, readily soluble in alcohol and ether, and distilling without decomposition. They dissolve in alkalis, yielding the salts of the corresponding hydroxy acids, and form brominated fatty acids with HBr, and amino acids or amides of γ-hydroxy acids with NH_3 (B. **23**, Ref. 234).

δ- and β-, but only a few α-lactones, from δ-, β-, and α-hydroxy acids, are also known. They show marked differences in the ease with which they are formed and in their stability, the γ-lactones being the most stable. (For α-Lactones, see B. 1891, **24**, 4070; for β, B. 1897, **30**, 1954, cf. Chap. XLVIII C.)

The formation of lactones by warming the isomeric unsaturated acids, $C_nH_{2n-2}O_2$, which contain the double bond in the

β-γ or γ-δ position, with HBr or with moderately concentrated H_2SO_4, is worthy of note, *e.g.*:



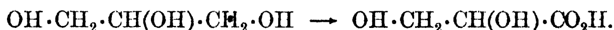
$$R \cdot CH:CH \cdot CH_2 \cdot CO_2H \rightarrow R \cdot CH \cdot CH_2 \cdot CH_2 \cdot CO.$$

(For details, see *Fittig* and his pupils, A. **208**, 37, 111; **216**, 26; **255**, 1, 275; **256**, 50; **268**, 110.)

The reaction is generally regarded as the addition of HBr or H_2O to the double bond, and then the elimination of the Br or OH in the γ-position with the H of the carboxyl group.

B. Polyhydric Monobasic Acids

Just as glycol on oxidation can yield the monohydroxy monobasic acid, glycollic acid, so the polyhydric alcohols on careful oxidation with nitric acid can yield polyhydroxy monobasic acids, *e.g.*:



$$OH \cdot CH_2 \cdot CH(OH) \cdot CH_2 \cdot OH \rightarrow OH \cdot CH_2 \cdot CH(OH) \cdot CO_2H.$$

They are usually designated according to the number of alcoholic hydroxyl groups present. This number can be determined by converting the acid, or better, its ester, into the acetyl derivative, and estimating the number of acetyl groups by analysis or by hydrolysis (p. 209).

In none of these acids do we find more than one OH group attached to the same carbon atom. All have the properties of monobasic acids and, in addition, the properties of polyhydric alcohols. Those which contain a hydroxyl group in the γ-position yield lactones.

Most of the compounds belonging to this class either crystallize badly or are gum-like. A number of these acids are formed by the cautious oxidation of the sugars or of the unsaturated acids, $C_nH_{2n-2}O_2$ (see p. 168).

I. DIHYDROXY MONOBASIC ACIDS

Glyceric acid (*Propane*-2:3-*diol*-1-*acid*), $OH \cdot CH_2 \cdot CH(OH) \cdot CO_2H$, is a syrupy liquid which is obtained by the cautious oxidation of glycerol. The molecule contains an asymmetric carbon atom, the artificial acid is optically inactive, but a *d*- and an *l*-modification are known (*Frankland*, J. C. S. 1891, 96).

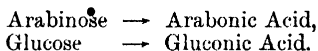
Various compounds obtained from natural sources are closely related to the dihydroxy acids, viz. serine, α-amino-β-hydroxy-

propionic acid, obtained by boiling silk glue with dilute acids; **ornithine**, $\alpha\delta$-diamino-valeric acid; and **lysine**, $\alpha\epsilon$-diamino-caproic acid, obtained by the hydrolysis of casein.

II. TETRA- AND PENTAHYDROXY MONOBASIC ACIDS

The tetra- and pentahydroxy acids, *e.g.* $OH \cdot CH_2 \cdot (CH \cdot OH)_3 \cdot CO_2H$ and $OH \cdot CH_2 \cdot (CH \cdot OH)_4 \cdot CO_2H$, are of particular importance, on account of their close connection with the simple sugars. They are obtained either by the cautious oxidation of the corresponding sugars, *e.g.* by means of bromine water: or by the reduction of the corresponding dibasic acids (saccharic acid, &c.); or, lastly, by the addition of hydrocyanic acid to the polyhydroxy aldehydes or ketones, just as lactic acid is formed from aldehyde. Conversely, the acids, in the form of their lactones, are on the one hand reconverted into the sugars by reduction with sodium amalgam; while, on the other hand, they are oxidized by nitric acid to the corresponding dibasic acids.

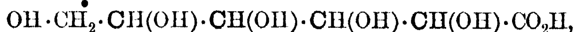
The acids are named according to the sugar to which they are related:


Arabinose → Arabonic Acid,
Glucose → Gluconic Acid.

(See Sugars, p. 310, &c.)

Some of the acids are known in the form of their lactones only. The phenyl-hydrazones are frequently made use of for their isolation.

A number of different acids, *e.g.* mannonic, gluconic, gulonic, galactonic, and talonic acid, have been obtained by the oxidation of the hexoses (p. 318) and by other methods. Investigation has shown that those acids all possess the same structural formula,


$$OH \cdot CH_2 \cdot CH(OH) \cdot CH(OH) \cdot CH(OH) \cdot CH(OH) \cdot CO_2H,$$

which is seen to contain 4 distinct asymmetric carbon atoms.

The acids are thus stereo-isomeric; their differences depend on the arrangement in space of the different radicals (cf. the Monosaccharoses, Chap. XIV, A.).

The number of stereo-isomerides possible is the same as for the sugars (the corresponding aldo-hexoses), viz. eight pairs of optically active isomerides and eight racemic compounds. Most, but not all, of these have been obtained.

Three extremely important methods have been employed (mainly by *E. Fischer*) for the preparation of these acids:—

1. Oxidation of the corresponding aldehyde (a sugar), *e.g.* ordinary glucose when carefully oxidized with chlorine- or bromine-water yields *d*-gluconic acid:

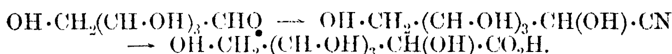


$$OH \cdot CH_2 \cdot (CH \cdot OH)_4 \cdot CH{:}O \longrightarrow OH \cdot CH_2 \cdot (CH \cdot OH)_4 \cdot CO \cdot OH.$$

2. From a stereo-isomeric acid by intramolecular transformation under the influence of high temperature, and generally in the presence of an organic base, *e.g.* *d*-gluconic heated with quinoline and water yields *d*-mannonic; galactonic → talonic. The reaction is a reversible one, and hence the final product is a mixture of the two acids, which can be separated by the difference in solubility of certain of their salts.

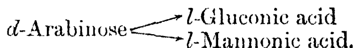
The name *epimerization* is given to this reaction which involves an inversion of two groups attached to the α-carbon atom.

3. The addition of hydrogen cyanide to a polyhydric aldehyde or ketone and subsequent hydrolysis, *e.g.*:



$$OH \cdot CH_2(CH \cdot OH)_3 \cdot CHO \longrightarrow OH \cdot CH_2 \cdot (CH \cdot OH)_3 \cdot CH(OH) \cdot CN \longrightarrow OH \cdot CH_2 \cdot (CH \cdot OH)_3 \cdot CH(OH) \cdot CO_2H.$$

It is obvious that an additional asymetric carbon atom is introduced by the addition of the HCN, and thus a mixture of two stereo-isomeric nitriles is formed, and on hydrolysis a mixture of two stereo-isomeric acids, *e.g.*:



This reaction is somewhat similar to the addition of HCN to acetaldehyde, the main difference is that the original compound is optically active, and hence its molecule is dissymmetric. By the addition of HCN two compounds are obtained, as a rule not in equal amounts, both of which are optically active, but do not stand in the relationship of object to mirror image.

C. Hydroxy Aldehydes

As examples, we have **glycollic aldehyde,** $OH \cdot CH_2 \cdot CH{:}O$, **aldol,** $CH_3 \cdot CH(OH) \cdot CH_2 \cdot CH{:}O$ (see p. 137), and **glyceric aldehyde,** $OH \cdot CH_2 \cdot CH(OH) \cdot CH{:}O$. The last-named is contained in glycerose, a product obtained by oxidizing glycerol with bromine water. Alkalis convert it into a mixture of sugars, $C_6H_{12}O_6$ (see α-Acrose). (For further examples of hydroxy aldehydes and ketones, cf. Monosaccharoses, Chap. XIV, A.)

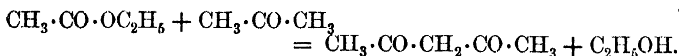
D. Dialdehydes

Glyoxal (*Ethane-dial*), CHO·CHO (*Debus*, 1856), is formed by the careful oxidation of alcohol, or better, of aldehyde; it possesses all the characteristic properties of aldehydes; one molecule of the aldehyde is capable of combining with two of hydrogen cyanide or of sodium hydrogen sulphite.

E. Diketones

1. **Diacetyl**, *Butane-dione*, *α-diketo-butane*, $CH_3·CO·CO·CH_3$, b.-pt. 87°–88°. This can be prepared by boiling iso-nitroso-methyl acetone, $CH_3·C(:N·OH)·CO·CH_3$, a product obtained by the action of nitrous acid on methyl ethyl ketone, with dilute H_2SO_4, when the oximino group is replaced by oxygen. It is a yellow-green liquid, its vapour having the colour of chlorine, and an odour similar to that of quinone (*v. Pechmann*, B. **20**, 3162; **24**, 3594; *Fittig* and his pupils, A. **249**, 182). Reduction converts it into dimethyl-ketol. Homologues are known (cf. B. **22**, 2115).

2. **Acetyl-acetone**, $CH_3·CO·CH_2·CO·CH_3$, is formed by the action of aluminium chloride upon acetyl chloride and subsequent decomposition of the aluminium compound, or better (B. **22**, 1009), by the action of sodium upon a mixture of ethyl acetate and acetone (see Aceto-acetic ester synthesis, p. 232):



$$CH_3·CO·OC_2H_5 + CH_3·CO·CH_3 = CH_3·CO·CH_2·CO·CH_3 + C_2H_5OH.$$

It is a liquid which boils at 137°.

3. **Acetonyl-acetone**, 2:5-*diketo-hexane*, $CH_3·CO·CH_2·CH_2·CO·CH_3$, may be prepared from monochlor-acetone and ethyl aceto-acetate (B. **17**, 2756); also from diaceto-succinic ester (B. **22**, 168, 2100). It is a liquid of pleasant odour, and boils at 188°.

These three compounds are the simplest representatives of the α-, β-, and γ-diketones, or of the 1:2-, 1:3-, and 1:4-diketones, *i.e.* of those diketones whose carbonyl groups are either next to one another (α-position), or separated by one carbon atom (β-position), or separated by two (γ-position).

As diketones they yield mono- and dioximes, and also mono- and dihydrazones. Such dihydrazones, and also those

from the dialdehydes, are termed **osazones**, *e.g.* **diacetyl osazone**.



$C_6H_5 \cdot NH \cdot N:CMe \cdot CMe:N \cdot NH \cdot C_6H_5$.

Osazones are also formed by the action of phenylhydrazine on polyhydroxy aldehydes or ketones, *e.g.* glucose and fructose, an atom of oxygen being at the same time taken up; they are mostly yellow in colour (cf. the phenyl-hydrazine compounds of the carbohydrates).

The diketones show the most varied behaviour on condensation. By the action of alkali on the α-diketones, they yield benzene derivatives (see Quinone); the β-diketones readily pass into pyrazole and isoxy-azole derivatives, and serve for the synthesis of derivatives of quinoline; while the γ-diketones are easily converted into derivatives of pyrrole, furane, and thiophene, and the δ-diketones into derivatives of pyridine and tetrahydrobenzene.

The constitution of the above compounds is usually deduced directly from their mode of formation, but as certain of them react as tautomeric substances (cf. Ethyl Aceto-acetate) special physical methods have also been used (cf. *W. H. Perkin*, J. C. S. 1892, 800).

F. Aldehydic Monobasic Acids

Glyoxalic acid (*Ethanal acid*), *glyoxylic acid*, $CHO \cdot CO_2H$, occurs in unripe fruits such as grapes, gooseberries, &c., and may be prepared by superheating dichloracetic acid, $CHCl_2 \cdot CO_2H$, with water, 2Cl being here exchanged for 2(OH), and water being eliminated. It crystallizes in rhombic prisms, dissolves readily in water, and is volatile with steam. The acid and most of its salts contain one molecule of water of crystallization, which points to the formula $CH(OH)_2 \cdot CO_2H$, analogous to that of chloral hydrate.

Glycuronic acid, $CHO \cdot [CH(OH)]_4 \cdot CO_2H$. The lactone of this acid forms colourless crystals, which melt at about 175°. The acid itself is obtained from saccharic acid by reduction with sodium amalgam. It is found as a camphor compound in the urine of dogs after camphor is administered to them.

G. Monobasic Ketonic Acids

Ketonic acids are compounds which contain both a carbonyl and a carboxylic group; they react as acids, and also as ketones;

thus, besides being capable of forming salts, esters, &c., they also combine with sodium bisulphite, yield oximes with hydroxylamine hydrochloride (see p. 141), are reduced by nascent hydrogen to hydroxy acids, and so on. The most important members of this class are **pyroracemic acid**, $CH_3 \cdot CO \cdot CO_2H$, **aceto-acetic acid**, $CH_3 \cdot CO \cdot CH_2 \cdot CO_2H$, and **lævulic acid**, $CH_3 \cdot CO \cdot CH_2 \cdot CH_2 \cdot CO_2H$.

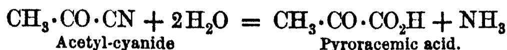
Constitution and Nomenclature.—The ketonic acids are characterized theoretically by the presence of carboxyl and of carbonyl, the latter being linked to carbon on both sides. They may be regarded either as fatty acids, in which a hydrogen atom of the alkyl group has been replaced by acyl, $R \cdot CO \cdot$, as indicated in the name aceto-acetic acid; lævulic acid is then β-aceto-propionic acid, and pyroracemic acid is aceto-formic acid; or they may be regarded as derived from the fatty acids by the replacement of the two hydrogen atoms of a $CH_2 \cdot$ group by an atom of oxygen.

In the latter case aceto-acetic acid is to be designated *β-ketobutyric acid*, or *butane-3-one-1-acid*. This last is the systematic name (Geneva Congress); the expression *one* indicates the presence of a ketonic group, and the number indicates the relative positions of the ketonic and carboxylic groups.

The *constitution* of a ketonic acid is, as a rule, easy to determine, either from its synthesis or from its transformation into the corresponding hydroxy acids of known constitution by means of nascent hydrogen.

The ketonic acids are usually divided into α, β, and γ, or 1, 2, and 3 ketonic acids, according to the relative positions of the carbonyl and carboxylic groups. $CH_3 \cdot CO \cdot CO_2H$, pyroracemic or pyruvic acid, is a type of an α-acid; $CH_3 \cdot CO \cdot CH_2 \cdot CO_2H$, aceto-acetic acid, is a type of a β-acid; and $CH_3 \cdot CO \cdot CH_2 \cdot CH_2 \cdot CO_2H$, lævulic acid, is a type of a γ-acid. The α- and γ-acids are relatively stable; many can be distilled without undergoing decomposition; but the β-acids are remarkably unstable, and readily lose carbon dioxide, yielding ketones. All the ketonic acids on careful reduction yield hydroxy acids.

Modes of Formation.—1. α-Ketonic acids are formed when the acyl cyanides are hydrolysed (*Claisen* and *Shadwell*) (cf. p. 186 and B. 1898, **31**, 1023):



$$\underset{\text{Acetyl-cyanide}}{CH_3 \cdot CO \cdot CN} + 2H_2O = \underset{\text{Pyroracemic acid.}}{CH_3 \cdot CO \cdot CO_2H} + NH_3$$

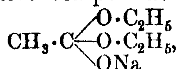
The constitution follows from this method of formation.

2. Aceto-acetic and other β-ketonic acids are obtained as esters by the action of sodium or sodium ethoxide on ethyl acetate and its homologues:



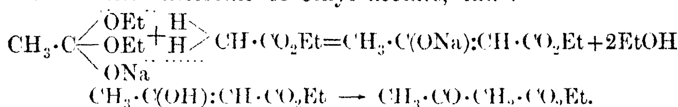
$$2(CH_3\cdot CO\cdot OC_2H_5) = CH_3\cdot CO\cdot CH_2\cdot CO\cdot OC_2H_5 + C_2H_5OH.$$

According to *Claisen* and *Lowman* (B. **20**, 651; **26**, 2130; **38**, 713), the ethyl acetate is first converted by the sodium ethoxide into an additive compound:



$$CH_3\cdot C \begin{cases} O\cdot C_2H_5 \\ O\cdot C_2H_5, \\ ONa \end{cases}$$

a derivative of ortho-acetic acid (p. 148), which then reacts with another molecule of ethyl acetate, thus:—



$$CH_3\cdot C \begin{cases} OEt \\ OEt \\ ONa \end{cases} + \begin{matrix} H \\ H \end{matrix} > CH\cdot CO_2Et = CH_3\cdot C(ONa){:}CH\cdot CO_2Et + 2EtOH$$

$$CH_3\cdot C(OH){:}CH\cdot CO_2Et \longrightarrow CH_3\cdot CO\cdot CH_2\cdot CO_2Et.$$

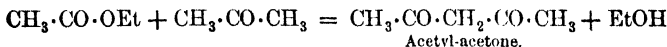
From the sodium salt thus obtained, the aceto-acetic ester can be liberated by acetic acid, probably first as the enolic compound, which is immediately transformed into the ketonic. Cf. B. 1903, **36**, 3674; 1905, **38**, 709; 1908, **41**, 1260.

As shown in the above formation of aceto-acetic ester, one molecule of ethyl acetate reacts with a second molecule. Many reactions of an analogous nature, in which the two reacting molecules are different, may be brought about in the same way by the aid of sodium ethoxide (*W. Wislicenus*, A. **246**, 306). Thus ethyl oxalate and ethyl acetate react in the presence of sodium ethoxide, yielding the sodio derivative of **ethyl oxal-acetate** (cf. *Dieckmann*, B. 1900, **33**, 2670):



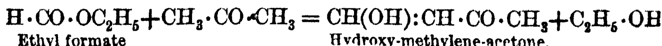
$$CO_2Et\cdot CO\,OEt + H\,CH_2\cdot CO_2Et = CO_2Et\cdot CO\cdot CH_2\cdot CO_2Et + EtOH.$$

Esters also readily react with ketones, with the formation of **diketones** (*L. Claisen*):



$$CH_3\cdot CO\cdot OEt + CH_3\cdot CO\cdot CH_3 = \underset{\text{Acetyl-acetone.}}{CH_3\cdot CO\cdot CH_2\cdot CO\cdot CH_3} + EtOH$$

When ethyl formate is employed, ketonic aldehydes are not obtained, but their structural isomers, hydroxy-methylene compounds; with acetone, for example, hydroxy-methylene-acetone, thus:—



$$\underset{\text{Ethyl formate}}{H\cdot CO\cdot OC_2H_5} + CH_3\cdot CO\cdot CH_3 = \underset{\text{Hydroxy-methylene-acetone.}}{CH(OH){:}CH\cdot CO\cdot CH_3} + C_2H_5\cdot OH$$

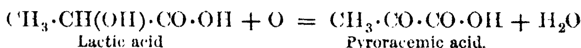
This condensation between esters, or between esters and ketones, in the presence of sodium ethoxide is usually known as *Claisen's* reaction, and is of extreme importance as a synthetical process. (For summary, see B. 1905, **38**, 709.)

In all cases, according to *Claisen*, the condensation is preceded by the formation of an additive compound between the sodium ethoxide and the ester. As a rule, metallic sodium and not sodium ethoxide is added to the ester (*e.g.* to ethyl acetate in the preparation of ethyl aceto-acetate), but the reaction only proceeds when the ester contains free alcohol, and can thus give rise to the ethoxide. The same chemist has shown (B. 1905, **38**, 693) that sodamide, $Na{\cdot}NH_2$, may be used in place of sodium ethoxide.

Michael (B. 1900, **33**, 3731, and 1905, **38**, 1922) considers the *Claisen* condensation proceeds in a different manner, and that it may be compared with the aldol condensation. (Compare also *Stoermer* and *Kippe* (B. 1905, **38**, 1953; 1922, **55**, 789).

3. Higher homologues of aceto acetic ester (β-ketonic acids) are easily obtained from it by the action of sodium ethoxide and alkyl halides (p. 236).

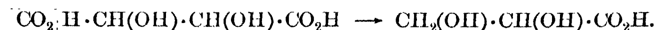
4. Ketonic acids are produced by the cautious oxidation of hydroxy acids containing the secondary alcoholic group:



$$\underset{\text{Lactic acid}}{CH_3{\cdot}CH(OH){\cdot}CO{\cdot}OH} + O = \underset{\text{Pyroracemic acid.}}{CH_3{\cdot}CO{\cdot}CO{\cdot}OH} + H_2O$$

α-**Ketonic Acids.**—**Pyruvic** or **pyroracemic acid**, $CH_3{\cdot}CO{\cdot}CO_2H$, is a liquid which is readily soluble in water, alcohol, and ether, boils with slight decomposition at 165°–170°, and smells of acetic acid and extract of beef. It is formed by the dry distillation either of tartaric or of racemic acid, hence its name.

In this decomposition carbon dioxide is probably first evolved and glyceric acid formed:



$$CO_2H{\cdot}CH(OH){\cdot}CH(OH){\cdot}CO_2H \longrightarrow CH_2(OH){\cdot}CH(OH){\cdot}CO_2H.$$

This then loses water, yielding pyruvic acid.

It may also be obtained by methods 1 and 4.

Pyroracemic acid has a tendency to polymerize. Nascent hydrogen reduces it to ethylidene-lactic acid:



$$CH_3{\cdot}CO{\cdot}CO_2H + 2H = CH_3{\cdot}CH(OH){\cdot}CO_2H.$$

It is a relatively strong acid owing to the negative nature

of the CO group, K = 0·56. It reacts as a ketone with phenyl-hydrazine, hydroxylamine, and hydrogen cyanide.

The **phenyl-hydrazone** crystallizes readily, melts at 190° when quickly heated, and is largely made use of in detecting the acid. The acid also resembles the ketones in the readiness with which it forms condensation products, yielding either benzene derivatives (B. **5**, 956), or—in presence of ammonia—those of pyridine.

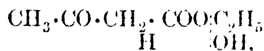
The electrolysis of a concentrated solution of the potassium salt proceeds in the normal manner, the $CH_3{\cdot}CO{\cdot}COO{\cdot}$ groups formed at the anode yield diacetyl and carbon dioxide (cf. Electrolysis of potassium-acetate solution), but secondary reactions also occur, and acetic acid is formed.

β-**Ketonic Acids.**—**Aceto-acetic acid,** $CH_3{\cdot}CO{\cdot}CH_2{\cdot}CO_2H$, is a strongly acid liquid, miscible with water, and breaking up into acetone and carbon dioxide when warmed. It is prepared by the cautious hydrolysis of its ethyl ester (B. **15**, 1376, 1871). Its aqueous solution is coloured violet red by ferric chloride. The Na- or Ca-salt is sometimes contained in urine (B. **16**, 2314). Its constitution as acetone-carboxylic acid follows from the products of decomposition.

The ethyl ester, ethyl aceto-acetate, or aceto-acetic ester, is prepared by the *Claisen* condensation (general method 2). It is liberated from the sodium derivative by the addition of acetic acid, and purified by distillation under reduced pressure. It boils at 181°, or at 71° under 12·5 mm. pressure, is only slightly soluble in water, but readily in alcohol and ether, and has a pleasant fruity odour. Ferric chloride colours its aqueous solution violet-red. Extremely characteristic are the products to which it can give rise on hydrolysis.

1. *Normal Hydrolysis.*—As an ester, it can be hydrolysed to the corresponding acid and alcohol, viz. aceto-acetic acid and ethyl alcohol. This reaction occurs only when it is extremely carefully hydrolysed in the cold with dilute alkali.

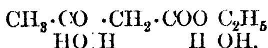
2. *Ketonic Hydrolysis.*—This hydrolysis is best accomplished by the aid of dilute sulphuric acid or baryta water,



$$CH_3{\cdot}CO{\cdot}\underset{H}{CH_2}{\cdot}\,COO\vdots\underset{OH,}{C_2H_5}$$

the products being acetone, carbon dioxide, and ethyl alcohol. It takes place also when the ester is heated with a little water at 200° (A. 1913, **398**, 242).

3. *Acid Hydrolysis.*—This takes place most readily when the ester is heated with concentrated alcoholic potash or soda,



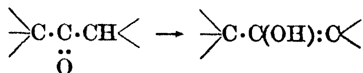
the products being acetic acid and ethyl alcohol.

Ethyl aceto-acetate has been represented by the formula $CH_3 \cdot CO \cdot CH_2 \cdot CO_2Et$, and undoubtedly numerous arguments can be brought forward in favour of this constitution; *e.g.* it reacts with acid sodium sulphite, with hydrogen cyanide, and with hydroxylamine as a ketone, and hence should contain the $C \cdot CO \cdot C$ group; a further argument for the ketonic constitution is to be found in the decomposition of the acid into acetone and carbon dioxide; on the other hand, with ammonia or amines it gives β amino, or substituted β-amino-crotonic acids, *e.g.* $CH_3 \cdot CH(NH_2):CH \cdot CO_2H$, and with phosphorus pentachloride it yields β-chloro-crotonic acid, $CH_3 \cdot CCl:CH \cdot CO_2H$. These latter reactions could be most readily explained by assuming the constitution $CH_3 \cdot C(OH):CH \cdot CO_2Et$, *i.e.* ethyl β-hydroxy-crotonate for ethyl aceto-acetate. The ester is thus a typical tautomeric substance, reacting as though it possessed two distinct constitutions, and a study of the chemical properties alone will not, as a rule, permit us to settle with certainty which of the two is the more probably correct.

The following suggestions have been made to account for the tautomerism:—

(*a*) The ester is really a mixture of the two distinct compounds.

(*b*) The pure ester is unstable, and although it may have the one constitution, *e.g.* ethyl aceto-acetate or *ketonic* constitution, in the presence of various reagents it is readily transformed into the isomeric compound with the *enolic* constitution, *i.e.* ethyl β-hydroxy-crotonate. This type of tautomerism is thus often spoken of as **keto-enolic tautomerism**, and is frequently met with (see Phloroglucinol, &c.). According to this view, it consists in the wandering of a hydrogen atom and a change in position of a double bond (desmotropism).



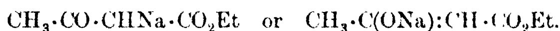
(*c*) According to *Van Laar*, the tautomerism is due to an oscillatory hydrogen atom, which cannot be regarded as per-

manently attached to C or to O, but as continually oscillating between the two.

Physical methods have been used for elucidating the constitution of such compounds. The most important of these are the molecular refraction (*Gladstone*, *Brühl*), the molecular magnetic rotation (*W. H. Perkin, Sen.*, J. C. S. 1892, 800), and the absorption of electric waves (*Drude*, B. 1897, **30**, 940). [Compare chapter on Relationship between Physical Properties and Chemical Constitution.] The conclusions arrived at from such a study are (*a*) that ethyl aceto-acetate is a mixture in chemical equilibrium of the ketonic and enolic forms, but consists mainly of the ketonic compound, and (*b*) that a rise of temperature favours the ketonic form. (See also *Baly* and *Desch*, J. C. S. 1904, 1029; 1905, 766.)

The metallic derivatives are enolic compounds.

1. **Ethyl Aceto-acetate as a Synthetical Reagent.**—One atom of hydrogen in the aceto-acetic ester molecule is readily replaceable by metals (*Geuther*; *Conrad*, A. **188**, 269). The **sodio derivative** is formed together with hydrogen on the addition of sodium, and also when an alcoholic solution of the ester is mixed with the calculated amount of sodium ethoxide in absolute alcohol:



$$CH_3 \cdot CO \cdot CHNa \cdot CO_2Et \quad \text{or} \quad CH_3 \cdot C(ONa){:}CH \cdot CO_2Et.$$

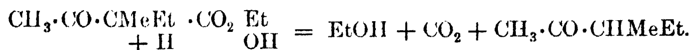
This sodio derivative forms long needles or a faintly lustrous loose white mass. The **copper salt** crystallizes in bright-green needles.

The sodium is readily replaced by alkyl radicals when the sodio derivative is heated with an alkyl bromide or iodide; sodium bromide or iodide is thus formed together with alkylated aceto-acetic esters, which are of great interest in various syntheses, *e.g.*: **ethyl methylacetoacetate**, $CH_3 \cdot CO \cdot CH(CH_3) \cdot CO_2C_2H_5$, and the corresponding **ethyl-** and **propyl-acetoacetic esters**, &c. In these compounds the hydrogen atom of the CH group may be again replaced by Na, and this again substituted by alkyl, with the production of dialkylated aceto-acetic esters, *e.g.*: **dimethylacetoacetic ester** or **ethyl dimethylacetoacetate**, $CH_3 \cdot CO \cdot C(CH_3)_2 \cdot CO_2C_2H_5$; **methylethylacetoacetic ester**, $CH_3 \cdot CO \cdot C(CH_3)(C_2H_5) \cdot CO_2C_2H_5$, and so on.

These alkylated aceto-acetic esters exactly resemble the mother substance, especially in the manner in which they can be decomposed by either the "ketonic hydrolysis" or the "acid hydrolysis" (cf. p. 235). The formation of ketone

largely predominates when dilute acid is employed, and of fatty acids when concentrated alkali is used.

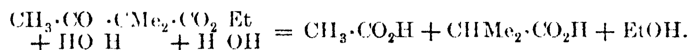
In the ketonic hydrolysis the alkyl groups introduced are left attached to a carbon atom of the acetone molecule, *e.g.*:



$$CH_3\cdot CO\cdot CMeEt\cdot \underset{+\,H}{}CO_2\,\underset{OH}{Et} = EtOH + CO_2 + CH_3\cdot CO\cdot CHMeEt.$$

This affords a very general method for the synthesis of some of the higher ketones.

In the acid hydrolysis the alkyl groups remain attached to a carbon atom, which is united to a carboxylic group, *e.g.*:



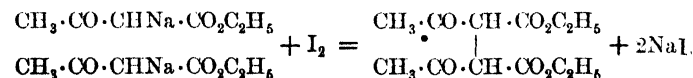
$$\underset{+\,HO\ H}{CH_3\cdot CO}\cdot \underset{+\,H}{CMe_2\cdot CO_2}\,\underset{OH}{Et} = CH_3\cdot CO_2H + CHMe_2\cdot CO_2H + EtOH.$$

This affords a simple method for synthesising any mono- or dialkylated acetic acid, *e.g.*: $CH_3\cdot CH_2\cdot CO_2H$; $C_2H_5\cdot CH_2\cdot CO_2H$; $(CH_3)(C_2H_5)CH\cdot CO_2H$; $(CH_3)(C_3H_7)CH\cdot CO_2H$. (Cf. Ethyl malonate synthesis, p. 215; also *Wislicenus* and his pupils, A. 186, 161.)

2. Acyl groups may be introduced in place of alkyl radicals into aceto-acetic ester by similar methods, *e.g.* from acetyl chloride, **diaceto-acetic ester**, $(CH_3\cdot CO)_2CH\cdot CO_2C_2H_5$. The product obtained varies with the conditions. When an acyl chloride reacts with the sodio-derivative of ethyl acetoacetate the chief product is the C-acyl derivative, viz. $(CH_3\cdot CO)(R\cdot CO)CH\cdot CO_2Et$, but when the free ester is treated with an acyl chloride in the presence of pyridine the isomeric O-acyl derivative is obtained, *e.g.* $R\cdot CO\cdot O\cdot C\cdot CMe:CH\cdot CO_2Et$. The O-derivatives, when heated or when warmed with potassium carbonate, are transformed into the isomeric C-compounds.

Ethyl chlorocarbonate and the sodio-derivative yield the O-derivative $CH_3\cdot C(O\cdot CO_2Et):CH\cdot CO_2Et$ together with a small amount of the C-derivative, **aceto-malonic ester**, $(CH_3\cdot CO)\cdot CH(CO_2C_2H_5)_2$; from monochloracetic ester, $CH_2Cl\cdot CO_2C_2H_5$, **aceto-succinic ester**, $CH_3\cdot CO\cdot CH(CH_2\cdot CO_2C_2H_5)(CO_2C_2H_5)$ may be similarly obtained (see Malonic and Succinic acids, and also the Synthesis of dibasic acids), &c.

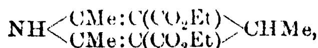
3. Iodine acts upon sodio-aceto-acetic ester, yielding **diaceto-succinic ester**:



$$\begin{matrix} CH_3\cdot CO\cdot CHNa\cdot CO_2C_2H_5 \\ CH_3\cdot CO\cdot CHNa\cdot CO_2C_2H_5 \end{matrix} + I_2 = \begin{matrix} CH_3\cdot CO\cdot CH\cdot CO_2C_2H_5 \\ | \\ CH_3\cdot CO\cdot CH\cdot CO_2C_2H_5 \end{matrix} + 2NaI.$$

4. In addition to the above-mentioned simple syntheses, a number of more complex syntheses may be effected by means of ethyl acetoacetate. Many of these lead to the formation of closed-chain compounds, and will be described in connection with the various groups of ring compounds. The following may be mentioned as the more important:—

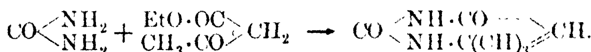
(*a*) *Hantzsch's* synthesis of pyridine derivatives, *e.g.* ethyl dihydrocollidine dicarboxylate,



by heating ethyl acetoacetate with aldehyde ammonia.

(*b*) The formation of **oxyuvitic acid** (a benzene derivative), $C_6H_2(CH_3)(OH)(CO_2H)_2$, by the action of chloroform on the sodio-derivative.

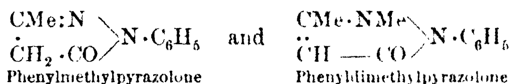
(*c*) The formation of **methyluracyl** by the condensation of ethyl acetoacetate with urea,



(See p. 297 and Synthesis of Uric Acid, p. 301.)

(*d*) The production of **furane** and **pyrrole derivatives** by heating ethyl diacetosuccinate (see Synthesis 3) with acids or with ammonia and amines.

(*e*) The synthesis of



by the condensation of ethyl acetoacetate with phenylhydrazine and methylphenylhydrazine respectively.

Chlor- and **dichlor-aceto-acetic esters**, which are very active chemically, are produced by the replacement of the H of the methylene group by Cl. The two methylene hydrogen atoms are also replaceable by the isonitroso group, :N·OH (by the action of N_2O_3), and by the imido group, :NH (cf. A. **226**, 294; B. **28**, 2683).

Lævulic acid, $CH_3·CO·CH_2·CH_2·CO_2H$, forms crystalline plates, melts at 33°, and boils at 239°. It is formed by the action of acids upon cane-sugar, lævulose, cellulose, gum, starch, and other carbohydrates (A. **175**, 181; **206**, 207), and has also been prepared synthetically. (For its constitution, cf. A. **256**, 314.) It is employed in cotton printing and for the preparation of anti-thermine, &c.

X. DIBASIC ACIDS

Dibasic acids are those which are capable of forming two series of salts, viz. acid and normal, and likewise two series of esters, chlorides, amides, &c. They are characterized by the presence of two carboxyl groups in the molecule.

A. Saturated Dibasic Acids, $C_nH_{2n-2}O_4$, or Acids of the Oxalic Series

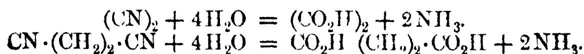
Name.	Formula.	Melting-pt.	K.
Oxalic	$CO_2H \cdot CO_2H$	Sublimes 150°–160°	10·0
Malonic	$CO_2H \cdot CH_2 \cdot CO_2H$	132°	0·016
Succinic	$CO_2H \cdot [CH_2]_2 \cdot CO_2H$	185°	0·0065
Glutaric	$CO_2H \cdot [CH_2]_3 \cdot CO_2H$	97·5°	0·0047
Adipic	$CO_2H \cdot [CH_2]_4 \cdot CO_2H$	149°	0·00371
Pimelic	$CO_2H \cdot [CH_2]_5 \cdot CO_2H$	105°	0·00323
Suberic.........	$CO_2H \cdot [CH_2]_6 \cdot CO_2H$	140°	0·00258

The above are solid crystalline compounds of strongly acid character, and most of them are readily soluble in water. When heated, they either yield an anhydride, or carbon dioxide is eliminated and a monobasic acid formed; but most of them can be volatilized *in vacuo*.

Formation.—1. By the oxidation of the di-primary glycols. (See table, p. 212.)

1*a*. By the oxidation of hydroxy-acids and, generally, of many complex compounds, such as fats, fatty acids, and carbohydrates.

2. By the hydrolysis of the corresponding nitriles; thus, oxalic acid is formed from cyanogen, and succinic acid from ethylene cyanide:

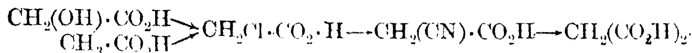


$$(CN)_2 + 4H_2O = (CO_2H)_2 + 2NH_3.$$
$$CN \cdot (CH_2)_2 \cdot CN + 4H_2O = CO_2H \cdot (CH_2)_2 \cdot CO_2H + 2NH_3.$$

Since ethylene cyanide is a glycol derivative, its conversion into succinic acid represents the synthesis from a glycol of an acid containing two atoms of carbon more than itself, *i.e.* the exchange of 2(OH) for $2(CO_2H)$, or the indirect combination of ethylene with $2(CO_2H)$.

3. By the hydrolysis of the cyano-fatty acids (p. 176), and consequently from the halogen fatty acids also. Thus chloro- or cyano-acetic acid yields malonic acid; β-iodo- (or cyano-) propionic acid, common succinic acid; and α-iodo- (or cyano-) propionic acid, methyl malonic acid.

A dibasic acid can therefore be formed from each hydroxy-acid by the exchange of OH for CO_2H, or indirectly from a fatty acid by the replacement of H by CO_2H. Thus:—



$$\left.\begin{array}{r}CH_2(OH)\cdot CO_2H\\ CH_3\cdot CO_2H\end{array}\right\rangle CH_2Cl\cdot CO_2\cdot H \rightarrow CH_2(CN)\cdot CO_2H \rightarrow CH_2(CO_2H)_2.$$

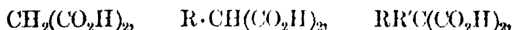
4. The homologues of malonic acid can be prepared from malonic acid itself by a reaction exactly analogous to the aceto-acetic ester synthesis (the "Malonic ester synthesis", p. 245).

The dibasic acids are also obtained by means of the aceto-acetic ester synthesis. Aceto-malonic and aceto-succinic acids, which have already been mentioned at p. 237, yield respectively malonic and succinic acids by the elimination of acetyl ("acid decomposition").

5. Higher homologues are obtainable by the electrolysis of the ethyl potassium salts (p. 242) of the simpler dibasic acids, *e.g.* adipic acid from potassium ethyl succinate.

The reaction is exactly analogous to the formation of ethane by the electrolysis of potassium acetate. For example, with potassium ethyl succinate the anions $CO_2Et\cdot CH_2\cdot CH_2\cdot \overset{-}{CO_2}\cdot$ and kations $\overset{+}{K}$ are present. When these become discharged at the electrodes during electrolysis, each $CO_2Et\cdot CH_2\cdot CH_2\cdot CO_2$ group splits up into carbon dioxide and the monovalent radical $CO_2Et\cdot CH_2\cdot CH_2\cdot$. Two such radicals then combine, yielding ethyl adipate, $CO_2Et\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CO_2Et$. The potassium formed at the cathode reacts with the water, yielding hydrogen and potassium hydroxide.

The *constitution* of the acids $C_nH_{2n-2}O_4$ is, as a rule, very easy to determine from the above-mentioned modes of formation, especially 2, 3, and 4. According to these, one has to decide between the malonic acids proper, *i.e.* malonic acid and its alkyl derivatives (p. 245), whose two carboxyl groups are both linked to one carbon atom:



$$CH_2(CO_2H)_2, \quad R\cdot CH(CO_2H)_2, \quad RR'C(CO_2H)_2,$$

and ordinary succinic acid and its homologues, which contain the carboxyls bound to two different carbon atoms.

The bivalent acid residues, C_2O_2 = **oxalyl**, $C_3H_2O_2$ = **malonyl**, and $C_4H_4O_2$ = **succinyl**, which are combined with the two hydroxyls, are termed **the radicals of the dibasic acids**, and are examples of bivalent acyl radicals.

Isomers.—Isomers of oxalic and malonic acids are neither theoretically possible nor actually known. We know, however, two succinic acids, viz.:



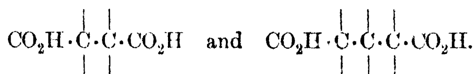
$$CO_2H \cdot CH_2 \cdot CH_2 \cdot CO_2H \quad \text{and} \quad CH_3 \cdot CH(CO_2H)_2.$$

The former corresponds with ethylene chloride and the latter with ethylidene chloride, from which they are respectively derived by the exchange of two chlorine atoms for two carboxyls. Hence the names ethylene- and ethylidene-succinic acids, or more commonly succinic acid and methylmalonic acid.

Since ethylene cyanide can be prepared from the chloride, the above derivation of ethylene-succinic acid is also an experimental one. This is not the case, however, with the isomeric acid, since, as a rule, when several chlorine atoms are bound to the same carbon atom, as in ethylidene chloride, they cannot be exchanged for cyanogen.

Behaviour.—Many of the dibasic acids, in the molecules of which the carboxyls are attached to different carbon atoms, yield intramolecular anhydrides by the elimination of a molecule of water from one of the acid. These anhydrides may be obtained either (1) by heating the acids alone, or (2) more generally by the action of phosphorus pentachloride, acetyl chloride, or carbonyl chloride upon the acids (B. **10**, 1881; **17**, 1285). They recombine slowly with water to form the free acids. This formation of anhydride is favoured by the presence of substituents in the molecule (B. **23**, 101, 620; **26**, 1925).

The elimination of water occurs most readily with succinic and glutaric acids and their substituted derivatives; in fact, with the acids containing a chain of 4 or 5 carbon atoms:



This is undoubtedly to be attributed to the spatial relationships of the atoms within the molecule. Assuming that the four valencies of a carbon atom are symmetrically distributed in space (*i.e.* directed towards the solid angles of a tetrahedron), then it can be readily seen by the aid of models that in acids of the above types the CO_2H groups are brought

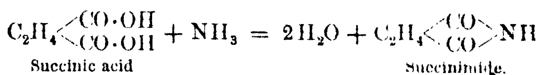
sufficiently near to one another for water to be eliminated, and for a closed ring to be formed (compare Polymethylene Derivatives).

The derivatives of the dibasic acids, *i.e.* their esters, amides, &c., show precisely the same characteristics as the analogous derivatives of the monobasic acids, especially in the readiness with which they are hydrolysed.

DERIVATIVES OF DIBASIC ACIDS

Derivatives.	Salts	Esters.	Chlorides.	Amides.
Acid.	$CO \cdot ONa$ $\dot{C}O \cdot OH$ Acid sodium oxalate.	$CO \cdot OC_2H_5$ $\dot{C}O \cdot OH$ Ethyl-oxalic acid.	$CO \cdot Cl$ $\dot{C}O \cdot O(H)$ (only known in derivatives).	$CO \cdot NH_2$ $\dot{C}O \cdot OH$ Oxamic acid.
Neutral or normal.	$CO \cdot ONa$ $\dot{C}O \cdot ONa$ Neutral sodium oxalate.	$CO \cdot OC_2H_5$ $\dot{C}O \cdot OC_2H_5$ Ethyl oxalate.	$CO \cdot Cl$ $\dot{C}O \cdot Cl$ Oxalyl chloride.	$CO \cdot NH_2$ $\dot{C}O \cdot NH_2$ Oxamide.

As in the case of the glycols, complications arise from the formation of mixed derivatives, *e.g.* partly ester and partly amide, as in the case of ethyl oxamate (p. 244), and also from the fact that many of the acids form imides. Such imides are derived from the hydrogen-ammonium salts of the acids by the elimination of two molecules of water, thus:—



$$C_2H_4<\begin{matrix}CO \cdot OH \\ CO \cdot OH\end{matrix} + NH_3 = 2H_2O + C_2H_4<\begin{matrix}CO \\ CO\end{matrix}>NH$$

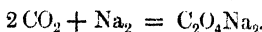
Succinic acid — Succinimide.

Like the amides they are readily hydrolysed (cf. Succinimide).

Oxalic acid (*Ethane diacid*), $(CO_2H)_2$, $2H_2O$, is one of the oldest known organic acids, and occurs as its acid potassium salt in many plants, especially in *Oxalis Acetosella* (wood-sorrel), and in varieties of Rumex, and as the free acid in varieties of Boletus, as normal sodium salt in varieties of Salicornia, and as calcium salt in rhubarb root, &c.

It may be prepared by a variety of different reactions.

1. By the direct combination of carbon dioxide with sodium at 360°:



$$2CO_2 + Na_2 = C_2O_4Na_2.$$

2. By quickly heating sodium formate to a high temperature:



$$2HCO_2Na = H_2 + C_2O_4Na_2.$$

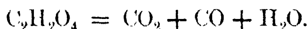
3. It is often met with as an oxidation product of relatively complex carbon compounds, *e.g.* by the oxidation of alcohol by permanganate, and of sugar, starch, wood, &c., by nitric acid. The oxidation of cane-sugar with concentrated nitric acid is often employed for the preparation of pure oxalic acid.

4. On the commercial scale, oxalic acid is manufactured by the fusion of cellulose (see Carbohydrates) in the form of sawdust with a mixture of sodium and potassium hydroxides at 200°–220° in flat iron pans. The sodium and potassium oxalates are extracted with water, then precipitated as calcium oxalate, and finally converted into the acid by treatment with the requisite amount of sulphuric acid. This method has become almost completely displaced by method 2.

It crystallizes from water in large, transparent, monoclinic prisms containing two molecules of water of crystallization. They slowly effloresce in the air, and readily become anhydrous when heated at 100°. At higher temperatures the acid partly decomposes into carbon dioxide and formic acid, and partly sublimes unaltered.

The acid is readily soluble in water, moderately in alcohol, and somewhat sparingly in ether. The aqueous solution decomposes when exposed to light.

Concentrated sulphuric acid decomposes it into carbon monoxide, carbon dioxide, and water:



$$C_2H_2O_4 = CO_2 + CO + H_2O.$$

Oxalic acid is stable as regards nitric acid and chlorine, but permanganate of potash or manganese dioxide in acid solution oxidizes it to carbonic acid:



$$C_2H_2O_4 + O = 2CO_2 + H_2O.$$

It is reduced by nascent hydrogen to glycollic acid.

The strength of an aqueous solution of the acid may be determined by titration with standard alkali, using phenol phthalein as indicator, or by means of standard permanganate in the presence of sulphuric acid.

Its *salts* are known as **oxalates**. The alkaline salts, both acid and normal, are readily soluble in water, the normal sodium

salt being the least so. The "**salt of sorrel**" of commerce is a mixture of C_2O_4HK and a salt, $C_2O_4HK + C_2O_4H_2 + 2H_2O$ (cf. p. 150). The **calcium salt**, $C_2O_4Ca + H_2O$ (or $3H_2O$), is insoluble in water and acetic acid, and serves for the recognition of oxalic acid. **Ferrous-potassium oxalate, $(C_2O_4)_2FeK_2$** $+ H_2O$, finds application in photography as a powerful reducing agent (the "oxalate developer").

Ethyl oxalate, $(CO \cdot OC_2H_5)_2$, which can be directly prepared from the anhydrous acid and ethyl alcohol without a catalytic agent, is liquid, while **methyl oxalate**, $(CO \cdot OCH_3)_2$, is a solid, crystallizing in plates which melt at 54°; both of them possess an aromatic odour, distil without decomposition, and are extremely readily hydrolysed. Partial hydrolysis, with alcoholic potash solution, produces **potassium ethyl-oxalate**, $COOK \cdot COOC_2H_5$, from which the free **ethyl-oxalic acid**, $COOH \cdot COOC_2H_5$, which is readily hydrolysed, and its chloride, **ethyl-oxalyl chloride**, $COCl \cdot COOC_2H_5$, can easily be prepared. Oxalic ester yields, with an excess of ammonia, oxamide, and with one equivalent the mixed derivative, **ammonium oxamate**, $COONH_4 \cdot CO \cdot NH_2$.

Oxalyl chloride, $(COCl)_2$, has been obtained by the action of excess of phosphorus pentachloride on ethyl oxalate. It is a liquid, b.-pt. 70°, and has a pungent odour (B. **41**, 3558).

Oxamide, $NH_2 \cdot CO \cdot CO \cdot NH_2$, the normal amide of oxalic acid, is obtained, among other methods, by the distillation of ammonium oxalate, by the partial hydrolysis of cyanogen, but is most readily obtained by the addition of ammonium hydroxide solution to ethyl oxalate. It is a white crystalline powder, is readily hydrolysed, and by the abstraction of water may be converted into cyanogen. When heated it sublimes unchanged.

Oxamic acid, $NH_2 \cdot CO \cdot CO \cdot OH$, the amic acid corresponding with oxalic acid, is prepared by heating ammonium hydrogen oxalate. It is a crystalline powder, sparingly soluble in cold water, possesses acid properties, and yields salts, esters, &c. It melts and decomposes at 210°.

Ethyl oxamate, *oxamethane*, $NH_2 \cdot CO \cdot CO \cdot OC_2H_5$, is a crystalline compound, and melts at 114°–115°. The action of PCl_5 on this compound is first to form $NH_2 \cdot CCl_2 \cdot CO \cdot OC_2H_5$, **ethyl-oxamine chloride**, which readily loses hydrogen chloride yielding $NH : CCl \cdot CO \cdot OC_2H_5$ and finally $N \vdots C \cdot CO \cdot OC_2H_5$, **cyano-carbonic ester**. Corresponding with oxamide we have **dimethyl-oxamide**, $CH_3 \cdot NH \cdot CO \cdot CO \cdot NHCH_3$, and

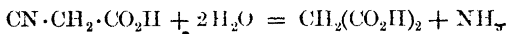
corresponding with oxamethane, **ethyl-dimethyl-oxamate,** $(CH_3)_2N\cdot CO\cdot CO\cdot OC_2H_5$, both of which were mentioned at p. 109.

Oximide, $\begin{matrix}CO\\ \cdot\\ CO\end{matrix}\!\!>\!NH$, is prepared by the action of PCl_5 upon oxamic acid. It forms colourless prisms readily soluble in water and of neutral reaction, is quickly hydrolysed by hot water, and is transformed into oxamide by the action of ammonia (B. **19**, 3228).

Cyanogen, $N\vdots C\cdot C\vdots N$, is the nitrile corresponding with oxalic acid (see p. 274).

Malonic acid, *Propane diacid*, $CH_2(CO_2H)_2$, occurs in beetroot as its calcium salt, and may be obtained by the following methods:—

(1) By the oxidation of malic acid by means of chromic acid, hence its name; (2) by the hydrolysis of malonyl-urea (p. 298), (*Baeyer*); (3) by the hydrolysis of cyano-acetic acid (*Kolbe*, *Müller*; A. **131**, 348; **204**, 121):



$$CN\cdot CH_2\cdot CO_2H + 2H_2O = CH_2(CO_2H)_2 + NH_3.$$

It crystallizes in large plates, dissolves readily in water, alcohol, and ether, melts at 132°, and decomposes when heated to a slightly higher temperature.

Ethyl malonate, *malonic ester*, $CH_2(CO\cdot OC_2H_5)_2$, is usually obtained by passing hydrogen chloride into a solution of cyano-acetic acid (from chloracetic acid) in absolute alcohol. It is a liquid of faint aromatic odour boiling at 198°, and having a remarkable similarity to aceto-acetic ester. Thus the hydrogen of the methylene group is replaceable by sodium, through the influence of the carbonyl groups CO, which are also bound to the methylene; and the resulting sodio-malonic ester readily exchanges the metal for alkyl when treated with an alkyl iodide. By this means the higher homologues of ethyl malonate, *e.g.* methyl-, ethyl-, propyl-, &c., malonic esters, are obtained. Further, the second hydrogen atom in these can be exchanged in exactly the same manner for sodium and then for alkyl, whereby dialkyl malonic acids are formed. This so-called "malonic ester" synthesis is an important method for the preparation of the higher dibasic acids, being applicable even in complicated cases. (Cf. *Conrad* and *Bischoff*, A. **204**, 121.) It is also of importance for the preparation of some of the higher fatty acids, as the substituted malonic

acids when heated above their melting-points lose carbon dioxide and yield fatty acids:

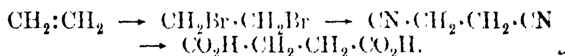


$$\frac{CH_3}{C_2H_5}{>}C(CO_2H)_2 \rightarrow \frac{CH_3}{C_2H_5}{>}CH\cdot CO_2H.$$

Malonic anhydride, carbon suboxide, C_3O_2, O:C:C:C:O, is formed when malonic acid is heated in a suitable apparatus at 140°–150°. (*Diels* and *Wolf*, B. 1907, 40, 355; cf. also 1906, 39, 689; *Staudinger* and *St. Bereza*, B. 1908, 41, 4461.) The yield is only 10–12 per cent, and acetic acid and carbon dioxide are also formed. It is a colourless liquid, b.-pt. + 7°, m.-pt. − 107°, and $D_{0°}^{0°}$ 1·11. It reacts readily with water, hydrogen chloride, dry ammonia, and aniline, yielding respectively malonic acid, malonyl chloride, malonamide, and malonanilide. It is stable at low temperatures, but decomposes rapidly at 100°.

Succinic acid, *Butane diacid, ethylene-succinic acid, symmetrical ethane-dicarboxylic acid* (from *succinum* = amber), $CO_2H\cdot CH_2\cdot CH_2\cdot CO_2H$. This acid has been known for a long time; its composition was determined by *Berzelius*. It exists in amber, in various resins and lignites, in many Compositae, in Papaveraceæ, in unripe wine grapes, urine, blood, &c.

It may be obtained by most of the general methods described on p. 239, *e.g.*: 1. By the hydrolysis of ethylene cyanide. This is an extremely important method, as it affords a synthesis of succinic acid and also establishes its constitution, since it can be shown that in ethylene dibromide the two bromine atoms are attached to distinct carbon atoms:



$$CH_2{:}CH_2 \rightarrow CH_2Br\cdot CH_2Br \rightarrow CN\cdot CH_2\cdot CH_2\cdot CN \rightarrow CO_2H\cdot CH_2\cdot CH_2\cdot CO_2H.$$

2. From β-iodo-propionic acid by conversion first into β-cyano-propionic acid and subsequent hydrolysis.

3. By the reduction of fumaric and maleic acids, $CO_2H\cdot CH{:}CH\cdot CO_2H$.

4. By heating its hydroxy-acids, malic or tartaric, with hydriodic acid:



$$CO_2H\cdot CH(OH)\cdot CH_2\cdot CO_2H + 2HI = CO_2H\cdot CH_2\cdot CH_2\cdot CO_2H + I_2.$$

5. It may also be obtained by the fermentation of the salts of these hydroxy-acids by means of certain micro-organisms, *e.g.* certain species of bacteria or yeasts.

It is also formed in small quantities as a by-product in the alcoholic fermentation of sugar, and by the oxidation of fats, fatty acids, and paraffins by means of nitric acid.

It is usually prepared from calcium malate according to 5, or by the distillation of amber.

6. It may also be synthesised from ethyl malonate. The sodio-derivative of this ester reacts not merely with alkyl iodides or bromides, but also with the esters of haloid fatty acids, *e.g.* ethyl bromoacetate.



$$(CO_2Et)_2CHNa + Br \cdot CH_2 \cdot CO_2Et = NaBr + (CO_2Et)_2 \cdot CH \cdot CH_2 \cdot CO_2Et.$$

The product is **ethyl ethane-tricarboxylate**, and when this is hydrolysed, alcohol, carbon dioxide, and succinic acid are formed. This method is of general interest, as various substituted succinic acids may be synthesised by this method. In place of sodio-ethyl malonate, the sodio-derivatives of esters of mono-substituted malonic acids may be used, and in place of ethyl bromo-acetate the esters of other halogen fatty acids, *e.g.* ethyl iodo-propionate or ethyl bromo-valerate. It has been shown (*Bone* and *Sprankling*, J. C. S. 1899, 839) that better yields can be obtained by using ethyl cyano-acetate and its derivatives in place of ethyl malonate and its derivatives.

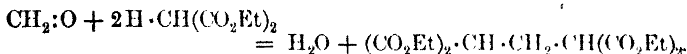
Properties.—It crystallizes in monoclinic prisms or plates with an unpleasant faintly acid taste, is readily soluble in water, melts at 185°, and boils at 235°, but is at the same time partially converted into its anhydride. (For its electrolysis, see pp. 49 and 240.) Is very stable towards oxidizing agents.

Of the salts of succinic acid, the **basic ferric salt**, obtained by the addition of a ferric salt to ammonium succinate, is used in analysis for the separation of the ferric and aluminic radicals. The **calcium** salt is soluble in water.

The derivatives of succinic acid correspond closely with those of oxalic, *e.g.* **succinamic acid**, $NH_2 \cdot CO \cdot CH_2 \cdot CH_2 \cdot CO \cdot OH$, is analogous to oxamic acid, and **succinamide**, $NH_2 \cdot CO \cdot CH_2 \cdot CH_2 \cdot CO \cdot NH_2$, to oxamide. There also exists, as in the case of other dibasic acids, an imide, **succinimide**, $C_2H_4\begin{matrix}<CO> \\ <CO>\end{matrix}NH$. The latter crystallizes in rhombic plates, and is formed by heating ammonium hydrogen succinate. The basic properties of the NH are so modified by the two carbonyl groups of the acid radical that the imido-hydrogen is

replaceable by metals, such as K, Ag, &c. (Cf. B. **25**, Ref. 283.) **Succinyl chloride** reacts as though it were **dichloro-butyro-lactone**, $C_2H_4<\begin{matrix}CCl_2\\CO-\end{matrix}>O$. It is a colourless liquid boiling at 190°, and is obtained by the action of phosphorus pentachloride (2 mols.) on the acid, or of 1 mol. on the anhydride. In many of its properties it resembles the acid chlorides, but on reduction yields **butyro-lactone**; with benzene and aluminium chloride it yields mainly **γ-diphenyl-butyro-lactone**, $C_2H_4<\begin{matrix}CPh_2\\CO-\end{matrix}>O$, and with zinc ethyl **γ-diethyl-butyro-lactone**. With NH_3 it yields but little amide, but with aniline gives the normal anilide (cf. *Auger*, Annales, 1891 [vi], **22**, 326; *Morell*, J. C. S. 1914, **105**, 1733). **Succinic anhydride,** $C_2H_4<\begin{matrix}CO\\CO\end{matrix}>O$, is best obtained by the action of acetic anhydride on the acid. It crystallizes in glistening plates, melts at 120°, and distils without decomposition. It slowly combines with water, yielding the acid; more readily with alkalis, and also with alcohols at a higher temperature, yielding the **acid esters,** *e.g.* $HO\cdot CO\cdot CH_2\cdot CH_2\cdot CO\cdot OEt$. This is the most convenient method for the preparation of acid esters. The other methods sometimes employed are: (*a*) the partial hydrolysis of the neutral ester, and (*b*) the partial esterification of the acid by means of very dilute solution of hydrogen chloride in the requisite alcohol (*Bone*, *Sudborough*, and *Sprankling*, J. C. S. 1904, 534).

Glutaric Acid, *Pentane diacid*, $CO_2H\cdot CH_2\cdot CH_2\cdot CH_2\cdot CO_2H$, may be obtained from glutamic acid (p. 258), and also by condensing formaldehyde with ethyl malonate in the presence of a small amount of diethylamine:



$$CH_2{:}O + 2H\cdot CH(CO_2Et)_2 = H_2O + (CO_2Et)_2\cdot CH\cdot CH_2\cdot CH(CO_2Et)_2.$$

This is a further example of the readiness with which aldehydes condense with compounds containing a methylene group adjacent to carbonyl or negative groups. The product, **ethyl propane-tetracarboxylate,** on hydrolysis yields ethyl alcohol, carbon dioxide, and glutaric acid. The last crystallizes in prisms, melts at 97°, is readily soluble in water, and yields **an anhydride, an imide,** &c. The imide can be obtained when piperidine is oxidized with hydrogen peroxide, and when distilled with zinc dust yields a small amount of pyridine.

Isomeric with glutaric acid is **methyl-succinic** or **pyrotartaric acid**, $CO_2H \cdot CHMe \cdot CH_2 \cdot CO_2H$, an acid closely resembling succinic acid, and obtained by dry distillation of tartaric acids.

The *s*-**dimethyl-** and *s*-**dibromo-succinic acids**, $CO_2H \cdot CHBr \cdot CHBr \cdot CO_2H$, occur in the same number of stereoisomeric modifications as the tartaric acids (p. 258).

Mono- and **dibromo-succinic acids**, $C_2H_3Br(CO_2H)_2$ and $C_2H_2Br_2(CO_2H)_2$, are easily prepared, and are valuable for the syntheses of the hydroxy-succinic acids.

Sodium reacts with ethyl succinate, yielding **ethyl succinylosuccinate**, a compound related to benzene. (Chap. XVII, G.).

Isosuccinic acid, *Methyl-propane diacid*, *ethylidene-succinic acid*, or *methyl-malonic acid*, $CH_3 \cdot CH(CO_2H)_2$, is formed by the malonic ester synthesis, or from α-chloro- (or iodo-) propionic acid (pp. 245 and 240). It is a solid, when heated decomposes into CO_2 and propionic acid, and yields no anhydride (p. 242).

Relative strengths of the dibasic acids:

	K
Oxalic...........................	10·0 (about)
Malonic..........................	0·163
Succinic.........................	0·0066
Glutaric.........................	0·0047

The strengths of alkylated succinic acids are not so very different from that of succinic acid, and those of alkyl glutaric acids are of the same order as that of glutaric.

B. Unsaturated Dibasic Acids

The unsaturated acids stand in the same relation to the saturated dibasic acids as acrylic acid does to propionic. As dibasic acids they yield derivatives analogous to those of oxalic acid, while as unsaturated compounds each molecule possesses, in addition, the property of combining with two atoms of hydrogen or halogen, or with one molecule of halogen hydride.

Common Methods of Formation.—1. By the elimination of water from the hydroxy dibasic-acids. Thus malic acid when distilled yields water and maleic anhydride, which volatilizes, and also fumaric acid, which remains behind:



$$CO_2H \cdot CH(OH) \cdot CH_2 \cdot CO_2H - H_2O = CO_2H \cdot CH{:}CH \cdot CO_2H.$$

The actual product obtained by the elimination of water

from malic acid varies considerably with the conditions of the experiment. Thus, when malic acid is maintained at a temperature of 140°–150° for some time, the chief product is fumaric acid; when the malic acid is rapidly heated at a higher temperature, maleic anhydride is largely formed.

Citric acid yields, in a similar way, CO_2, H_2O, itaconic acid, $CH_2{:}C(CO_2H){\cdot}CH_2{\cdot}CO_2H$, and citraconic anhydride (methylmaleic anhydride).

2. By the separation of halogen hydride from the monohaloid derivatives of succinic acid and its homologues, *e.g.* monobromo-succinic acid yields fumaric, thus:—



$$CO_2H{\cdot}CHBr{\cdot}CH_2{\cdot}CO_2H - HBr = CO_2H{\cdot}CH{:}CH{\cdot}CO_2H.$$

3. Fumaric acid has been prepared synthetically from acetylene di-iodide, just as succinic acid has been from ethylene dibromide.

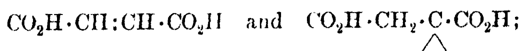
Constitution.—The acids of this series may be regarded as dicarboxylic acids of the olefines, *e.g.* fumaric and maleic acids, $C_2H_2(CO_2H)_2$, as those of ethylene. Their mode of formation 1 corresponds exactly with the production of ethylene from alcohol, or with that of acrylic from ethylene lactic acid, while 2 agrees with that of ethylene from ethyl iodide.

Maleic acid (*cis-Butene diacid*), $CO_2H{\cdot}CH{:}CH{\cdot}CO_2H$, crystallizes in large prisms, possesses a grating, nauseous acid taste, and is very readily soluble in cold water. It distils unchanged, excepting for partial transformation into maleic anhydride. It is conveniently prepared by heating the acetyl derivative of malic acid (see p. 256), or from fumaric acid and $POCl_3$ (A. **268**, 255).

Fumaric acid (*trans-Butene diacid*), $C_2H_2(CO_2H)_2$, crystallizes in small prisms with a strong, purely acid taste, and is almost insoluble in cold water. It does not melt, but sublimes at about 200° with formation of maleic anhydride. It occurs in *Fumaria officinalis*, various fungi, truffles, Iceland moss, &c., and is obtained from maleic acid either by prolonged heating of the latter at 130°, or by the action upon it of hydrobromic or other acids. (For its preparation, see A. **268**, 255.)

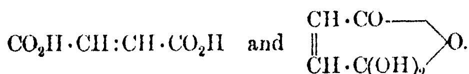
Both acids are converted into esters when their silver salts are heated with alkyl iodide, and these esters stand in very close relationship to one another, as do the free acids; thus ethyl maleate is changed into ethyl fumarate when warmed with iodine, and the latter ester is formed by saturating an alcoholic solution of maleic acid with dry hydrogen chloride.

Isomerism of Fumaric and Maleic Acids.—The isomerism of these two acids is a problem which has attracted the attention of numerous chemists. Attempts were first made to account for the difference by polymerism or structural isomerism, *e.g.* *Fittig* has suggested



but isomerism of this type is impossible, since both acids when oxidized yield one or other of the tartaric acids $CO_2H \cdot CH(OH) \cdot CH(OH) \cdot CO_2H$.

Anschutz has brought forward the formulæ

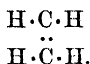


Such a formula as the latter is not at all probable, as in this case maleic acid, which is the stronger acid (K = 1·17, and for fumaric K = 0·093), would not possess a carboxylic, but merely a hydroxy lactone structure (*Wegscheider*, B. 1903, **36**, 1543). This formula is also found to be quite untenable when the products of bromination and of oxidation are considered.

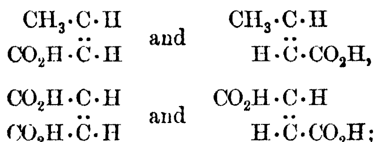
The fact that the two acids are structurally identical, and must both be represented as ethylene dicarboxylic acids, is now generally recognized, and the conclusion is largely based on the following facts:—(1) Both acids when reduced with sodium amalgam yield ordinary succinic acid. (2) Both acids combine with hydrogen bromide, yielding the same bromosuccinic acid. (3) Both acids combine with water at moderate temperatures, yielding the same malic acid. In most of these additive reactions the maleic acid reacts somewhat more readily than the fumaric, and is at the same time partially transformed into fumaric. (4) When carefully oxidized, the two acids yield stereo-isomeric tartaric acids, maleic being transformed into meso-tartaric, and fumaric into racemic acid. (5) Similarly, on addition of bromine they yield stereo-isomeric dibromo-succinic acids.

As the two acids are structurally identical, the isomerism can only be accounted for by a different spatial relationship of the atoms within the molecule. The stereo-isomerism of these unsaturated compounds is quite distinct from that of the saturated compounds, such as lactic and tartaric acids.

We are forced to assume that in saturated compounds where two C atoms are united by a single bond, there is free rotation around the axis represented by the bond; otherwise, the number of isomerides C a b c · C d e f, or even C a a b · C a a b, would be much greater than what is actually found.* When, however, the two carbon atoms become united by a so-called double bond, free rotation is completely prevented, and we have the centres of gravity of the two C atoms and of the four substituents all lying in the same plane, viz. the plane of the paper, *e.g.* C_2H_4 may be represented as



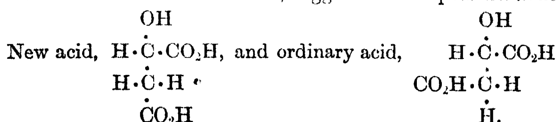
No stereo-isomerism is possible with such a compound, nor yet with any compound in which the 2 radicals attached to the one carbon atom are the same, *e.g.* $CH_2{:}CCl·CO_2H$; but immediately each carbon atom has 2 different radicals attached to it, isomerism is theoretically possible, *e.g.* crotonic acid, $CH_3·CH{:}CH·CO_2H$, and maleic acid, $CO_2H·CH{:}CH·CO_2H$, viz.:



and similarly for oleic and elaidic acids, erucic and brassidic acids, cinnamic and allocinnamic acids and its derivatives, and also for numerous other compounds.

As the centres of gravities of the carbon atoms and of their substituents all lie in one plane, the molecules are not perfectly asymmetric, and therefore possess no optical activity, and cannot be resolved into optically active components.

* There are a few instances of saturated compounds in which it has been suggested that free rotation does not occur. Thus, in 1898, *Aberson* (B., **31**, 1432), in order to account for the existence of a malic acid which had been isolated from certain species of *Echeveria*, but which was not identical with the known *d-l* and *r* malic acids, suggested the representations:—



A few exceptions to this generalization were at one time supposed to exist. Thus it was stated that an optically active solution of citraconic acid, $CO_2H\cdot CMe:CH\cdot CO_2H$, was obtained by the growth of certain fungi on the liquid. *Le Bel* (1894) was able to show that by the addition of water to the unsaturated acid, methyl malic acid is formed and is then attacked by the organism. Similarly the slight activity attributed to cinnamene, chlorofumaric, and chloromaleic acids has been shown to be due to small amounts of impurities (*Perkin*, J. C. S. 1888, 695). *Erlenmeyer* still claims to have obtained optically active cinnamic acids (cf. Chap. XXVI, A. 2).

The two isomerides are not so closely related to one another as *d*- and *l*-valeric acids, or as *d*- and *l*-tartaric acids; as a rule, they differ entirely as regards their ordinary physical properties, *e.g.* crystalline form, solubility, melting-point, water of crystallization, dissociation constant, &c., and in many cases considerable differences in chemical properties are met with, *e.g.* maleic acid yields an anhydride and fumaric acid does not. As a rule, one of the isomerides is less stable than the other, and under suitable conditions, *e.g.* influence of (*a*) heat, (*b*) light, (*c*) chemical reagents, especially small amounts of halogens or halogen hydracids, the labile compound is transformed into the stable. With certain pairs of isomerides the transformation is mutual, so that whichever of the two we start with we obtain, under the conditions enumerated above, a mixture of the two in chemical equilibrium.

As examples of the transforming action of heat we have the following:—Fumaric ⟶ maleic; allocinnamic ⟶ cinnamic; angelic ⟶ tiglic, and either chloro-fumaric, $CO_2H\cdot CCl:CH\cdot CO_2H$, or chloro-maleic acid heated separately yields a mixture of the two. The effect of exposure to sunlight is often identical with the action of heat, but not always so, *e.g.* ethyl benzylaminocrotonate, $\genfrac{}{}{0pt}{}{CH_3}{CH_2Ph\cdot NH}{>}C:CH\cdot CO_2Et$, exists in two stereo-isomeric modifications melting at 79° and 21°; the effect of heat is to transform the higher melting ester into the lower melting, and the effect of sunlight is the exact opposite. As examples of the influence of chemicals, we have the action of small amounts of nitrous acids in transforming oleic into elaidic and erucic into brassidic acids. Similarly, small amounts of bromine will transform dimethyl maleate into dimethyl fumarate.

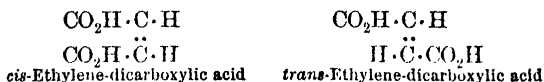
Ultra-violet light, on the other hand, by the addition of

energy, transforms the stable into the labile modification, *e.g.* cinnamic acid into allocinnamic acid, and often the most convenient method of preparing the labile form is to expose the stable compound to the action of the rays from a quartz mercury vapour lamp (*Stoermer*, B. 1909, 4865; 1911, 637; 1912, 3099; 1914, 1786, 1795, 1863; A. 1915, **409**, 13).

Skraup has shown that either sulphur dioxide or hydrogen sulphide alone is unable to transform maleic into fumaric, but that a mixture of the two will bring about the transformation. The chemical reaction between the H_2S and SO_2 may be regarded as a type of detonator which starts the transformation in the maleic acid. All chemical reactions, however, cannot act in the same manner as catalysts. The salts of maleic acid, *e.g.* copper maleate, when decomposed by hydrogen sulphide yield fumaric acid or a mixture of fumaric and maleic acids, although, as stated above, the sulphide itself is incapable of transforming free maleic acid into fumaric. Sodium thiosulphate alone brings about the isomeric change, and potassium in dry ether isomerises methyl maleate. A small amount of a primary or secondary amine, *e.g.* piperidine brings about the change in a few seconds. (J. C. S., 1930, 213.)

The exact method of transformation is not known. It may be (*a*) that the two radicals attached to the one carbon atom actually exchange positions directly; (*b*) the two carbon atoms may only be in a state of strain, and under the influence of light, heat, &c., a rotation through an angle of 180° may occur; or (*c*) in changes brought about by chemical agents the agent employed may first form an additive compound and then be subsequently removed, but this view has been shown to be impossible in many cases by *Anschutz*, *Fittig*, and *Michael*. *Terry* and *Eichelberger* (J.A.C.S., 1925, 1067, 1402) suggest the change of the covalent double linking to a semipolar linking.

The system of nomenclature adopted to distinguish between the two isomerides is to term the compound in which two similar substituents are on the same side of the molecule the **cis** compound, and the isomeride in which the two similar radicals are on opposite sides of the molecule the **trans**:

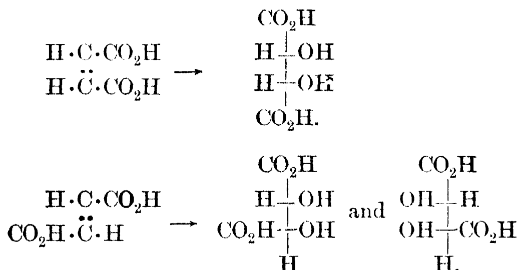


cis-Ethylene-dicarboxylic acid **_trans_-Ethylene-dicarboxylic acid**

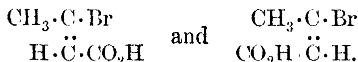
In cases where it has not been found possible to ascertain which of the two known compounds has the *cis* configuration

and which the *trans*, the ordinary name is given to the one and the prefix *iso*, or better, *allo*, to the other, *e.g.* crotonic and isocrotonic acids, cinnamic and allocinnamic acids.

Determination of Configuration.—In the case of fumaric and maleic acids this has been accomplished with a considerable degree of certainty. The arguments used for the *cis* configuration of maleic and the *trans* configuration of fumaric are briefly: (*a*) Maleic acid when heated, or treated with dehydrating agents, readily yields an anhydride (cf. Succinic anhydride), $\begin{matrix} CH \cdot CO \\ \ddot{C}H \cdot CO \end{matrix} \!\! > \! O$, which can combine with water to re-form maleic acid. Fumaric acid yields no distinct anhydride of its own. (*b*) Maleic acid when oxidized yields meso-tartaric acid, whereas fumaric acid yields racemic acid (see p. 262):



The configurations of other pairs of olefine stereo-isomerides have not been determined with the same degree of certainty, and many of the methods described in text-books as being available for this purpose cannot be relied on, *e.g.* of two stereo-isomeric *α*- or *β*-halogenated compounds, the one which has the halogen in the *cis*-position with respect to a hydrogen atom will lose halogen hydracid more readily under the influence of alkali, *e.g.*:



In many cases it is probable that exactly the reverse holds good.

Similarly it was assumed that by the addition of hydrogen, chloride, bromine, iodine, or their hydracids to an acetylene derivative, the addenda, *e.g.* two bromine atoms or one bromine

and one hydrogen, assume the cis positions in the olefine compound formed. It has been conclusively proved that acetylene-dicarboxylic acid with halogen hydracids yields monohalide derivatives of fumaric and not maleic acid (*Michael*, J. pr., 1892, **46**, 210; 1895, **52**, 352). According to *Garner* (C. N. 1919, **119**, 16), trans addition and trans elimination are the rule and not the exception, and can be accounted for by *Bohr's* theory of the arrangement of the atoms and electrons within the molecule.

An admirable account of the stereo-chemistry of olefine derivatives will be found in *Werner's* "Stereochemie", 1904, pp. 179–227. Compare also *Frankland*, J. C. S. 1912, **101**, 673; *Reich*, J. pr., 1914, **90**, 177.

For higher homologues, see *Fittig*, B. **26**, 40.

Acetylene-dicarboxylic acid, *Butine diacid*, $CO_2H \cdot C \vdots C \cdot CO_2H$, is a type of an acetylenic acid; it is obtained by the elimination of two molecules of hydrogen bromide from one of dibromo-succinic acid. It possesses the characteristic properties of a dibasic acid, and also of an unsaturated compound, but does not yield metallic derivatives of the type of silver acetylene. It readily loses carbon dioxide, yielding propargylic acid, $CH \vdots C \cdot CO_2H$. **Diacetylene-dicarboxylic acid**, $CO_2H \cdot C \vdots C \cdot C \vdots C \cdot CO_2H$, and **tetracetylene-dicarboxylic acid**, *Decatetrine diacid*, $CO_2H \cdot C \vdots C \cdot C \vdots C \cdot C \vdots C \cdot C \vdots C \cdot CO_2H$, have been prepared by *Baeyer* (B. **18**, 678 and 2269). With increasing length of chain they show an increasing tendency to explode. (For *Baeyer's* theory of explosions, see B. **18**, 2277.)

C. Hydroxy Dibasic Acids

1. **Tartronic acid**, *Propanol diacid*, *hydroxy-malonic acid*, $OH \cdot CH \cdot (CO_2H)_2$, forms large prisms ($+ \frac{1}{2}H_2O$), and is easily soluble in water, alcohol, and ether. It cannot be distilled unchanged, since it breaks up on heating into carbon dioxide and glycolide. As hydroxy-malonic acid it may be prepared by the action of moist silver oxide on chloromalonic acid. It may also be obtained by the reduction of the corresponding ketonic acid, mesoxalic acid, $CO(CO_2H)_2$, and also by the oxidation of glycerol with permanganate.

2. **Malic acid**, *Butanol diacid*, *hydroxy-succinic acid*, $CO_2H \cdot CH_2 \cdot CH(OH) \cdot CO_2H$ (*Scheele*, 1785), is very widely distributed in the vegetable kingdom, being found in unripe apples, sorb-apples, grapes, barberries, mountain-ash berries, quinces, &c.

Some of the simpler methods of formation are quite analogous to those employed in the case of hydroxy monobasic acids, *e.g.* (1) by the action of moist silver oxide on bromo-succinic acid; (2) by the reduction of tartaric or racemic acid with HI, and of oxal-acetic acid (pp. 232 and 269) with sodium-amalgam; (3) by the action of nitrous acid on the corresponding amino acid, aspartic acid; and (4) by the addition of the elements of water to fumaric or maleic acid under the influence of aqueous sodium hydroxide.

It crystallizes in hygroscopic needles, is readily soluble in water and alcohol, but only sparingly in ether. It melts at 100°, and when it is distilled, maleic anhydride passes over and fumaric acid remains in the retort (p. 250). K = **0·04.**

The molecule of malic acid contains an asymmetric carbon atom, and thus the acid should exist in two optically active and a racemic modification. The acid obtained from natural sources, *l*-malic acid, is lævo-rotatory in dilute solution, but the rotation diminishes as the concentration increases. With a 34-per-cent solution at 20° no optical activity is shown, and with more concentrated solutions dextro-rotation is exhibited. The acid obtained synthetically is optically inactive and constitutes the racemic form, and it has been resolved into optically active modification by the usual methods (p. 263), (B. 1898, **31**, 528).

The alkali salts and the acid calcium salt of malic acid are readily soluble in water, while the normal calcium salt is only sparingly soluble.

The constitution follows from its methods of preparation, from the fact that it is readily reduced to succinic acid, and that its esters react with acetic anhydride, yielding mono-acetyl derivatives.

Amides and Amines of Malic Acid.—Like glycollic acid, malic acid forms—as an acid—amides (saponifiable), and—as an alcohol—an amine (not saponifiable). The amides are:—

Malamide, $NH_2\cdot CO\cdot CH(OH)\cdot CH_2\cdot CO\cdot NH_2$, crystallizing in prisms, and **malamic acid,** $CO_2H\cdot CH_2\cdot CH(OH)\cdot CO\cdot NH_2$, the latter being only known as ethyl ester. The amino-acid, **aspartic acid,** $CO_2H\cdot CH(NH_2)\cdot CH_2\cdot CO_2H$, unites in itself, like glycocoll, the properties of a base and of an acid, but the acid character predominates. Its acid amide, **asparagine,** $CO_2H\cdot CH(NH_2)\cdot CH_2\cdot CO\cdot NH_2$, which is isomeric with malamide, is very widely distributed in the vegetable kingdom, being present in the young leaves of trees, in beet-root, potatoes, the shoots of peas, beans, and vetches, and in

asparagus; it was first found in the last-named vegetable in the year 1805. It forms glistening rhombic prisms ($+ H_2O$), is readily soluble in hot water, but insoluble in alcohol and ether, and yields aspartic acid when hydrolysed. It is lævo-rotatory.

A dextro-rotatory asparagine has likewise been obtained from the shoots of vetches (B. **20**, Ref. 510); it possesses a sweet taste, and unites with the lævo-rotatory compound to an inactive modification. For the synthesis of the asparagines and their constitution, see *Piutti*, B. **22**, Ref. 241 and 243.

Aspartic acid, *amino-succinic acid*, is present in beet molasses, and forms an important product of the decomposition of proteins with acids or alkalis. It has been synthesized, *e.g.* from bromo-succinic acid and ammonia, and crystallizes in small rhombic plates readily soluble in hot water. It exists in optically active modifications, which differ in taste and are convertible the one into the other (B. **20**, R. 510). Nitrous acid transforms both aspartic acid and asparagine into malic acid.

Glutamic acid, *a-amino-glutaric acid*, $CO_2H \cdot CH(NH_2) \cdot CH_2 \cdot CH_2 \cdot CO_2H$, and **glutamine** correspond with aspartic acid and asparagine. The former is found in beet-root and in the shoots of the vetch and gourd, while the latter is produced, together with aspartic acid and leucine, by boiling proteins with dilute sulphuric acid.

D. Dihydroxy Dibasic Acids

These acids are characterized by the presence of two hydroxyl radicals in the molecule in addition to two carboxyls.

Tartaric acid, *Butane-diol diacid*, *dihydroxy-succinic acid*, $CO_2H \cdot CH(OH) \cdot CH(OH) \cdot (CO_2H)$, exists in four distinct modifications.

1. *d-* or **Dextro-tartaric acid**, m.-pt. 170°.

2. *l-* or **Lævo-tartaric acid**, *anti-tartaric acid*, m.-pt. 170°.

3. **Racemic acid**, *d-l-tartaric acid*, *para-tartaric acid*, m.-pt. 206°.

4. *i-* or **Inactive tartaric acid**, *meso-tartaric acid*, m.-pt. 143°.

The constitution of these acids follows from their relationship to succinic acid, from their methods of formation, and from the fact that their esters with acetic anhydride yield *diacetyl* derivatives.

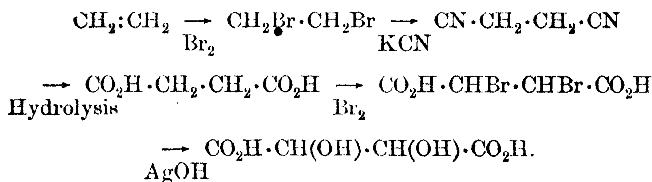
Solutions of equal concentration of the two first of these

acids turn the plane of polarization of light in an equal degree, but in opposite directions. By their union the inactive racemic acid is formed, and this can, conversely, be separated into its components. The fourth tartaric acid, likewise inactive, cannot be resolved in this way.

The common tartaric acid found in nature is optically active, and is the *d*-tartaric acid, whereas the acids obtained synthetically are optically inactive, viz. racemic acid or meso-tartaric acid, or a mixture of both, *e.g.* dibromo-succinic acid with moist silver oxide yields a mixture of racemic and meso-tartaric acids.

Fumaric acid when oxidized with permanganate is converted into racemic acid, and maleic acid by a similar process into meso-tartaric acid (p. 255). Glyoxal cyanhydrin (p. 229) when hydrolysed yields racemic acid, and finally, mannitol when oxidized with nitric acid yields racemic acid, and sorbitol meso-tartaric acid.

Synthesis:



$$CH_2{:}CH_2 \xrightarrow[Br_2]{} CH_2Br{\cdot}CH_2Br \xrightarrow[KCN]{} CN{\cdot}CH_2{\cdot}CH_2{\cdot}CN$$

$$\xrightarrow[\text{Hydrolysis}]{} CO_2H{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H \xrightarrow[Br_2]{} CO_2H{\cdot}CHBr{\cdot}CHBr{\cdot}CO_2H$$

$$\xrightarrow[AgOH]{} CO_2H{\cdot}CH(OH){\cdot}CH(OH){\cdot}CO_2H.$$

Stereo-isomerism of the Tartaric Acids.—The isomerism of the tartaric acids is of much the same type as that discussed in the case of active valeric and of α-lactic acid. A glance at the constitutional formula for the acids shows the presence of 2 asymmetric carbon atoms; to each of these 2 atoms are attached the radicals H, OH, and CO_2H, and the remaining valency of each carbon is employed in attaching it to the other carbon atom.

A compound of this general type, C(a, b, c) · C(a, b, c), is known as a compound containing 2 similar asymmetric carbon atoms. If one valency of each carbon is employed in uniting the 2 carbon atoms together, then the 3 radicals, a, b, c, which are attached to the remaining three valencies of a carbon atom, may be arranged in two distinct ways, viz. a↷b c, positive order, and a↶c b, negative order.

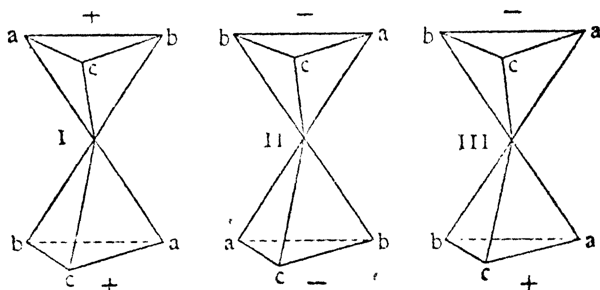
The following combinations are thus possible:—

	1	2	3	4
	+	−	+	−
	+	−	−	+

or 1 2 3 4

But Nos. 3 and 4 must be identical, as the radicals attached to the 2 asymmetric carbon atoms are identical.

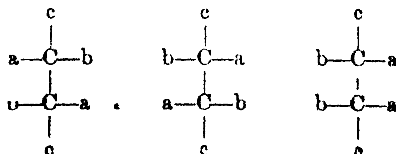
These spatial relationships may be represented:

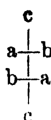
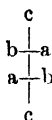
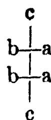


where a = H, b = OH, and c = CO_2H.

Note.—At first sight it appears as though the radicals a, b, c in the lower half of fig. 1 were arranged in the − and not the + order, as indicated. It must be remembered, however, that each part of the molecule must be looked at from the same point of view; and if we take the order of the radicals in the upper tetrahedron when arranged so that the solid angle which represents the point of attachment to the second tetrahedron is pointed down, then we must regard the second tetrahedron from the same point of view, *i.e.* we must turn the figure upside down. It is then seen that the arrangement in the lower half of the molecule is the +.

Instead of using the above cumbrous figures, it is usual to regard such models as projected upon a plane surface, and to use the projections thus obtained (*E. Fischer*, B. 1891, 24, 2684):

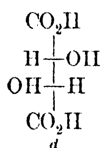
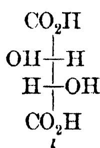
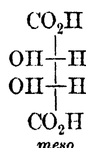


or   

Note.—The manner in which these projection formulæ are obtained can be best seen by means of models.

A comparison of the three configurations at once shows that Nos. I and II are enantiomorphous, and are related to one another as object to mirror image; they should therefore represent the two optically active tartaric acids, and the compound of the two should represent the molecule of racemic acid. No. III has a plane of symmetry, and should therefore represent the non-resolvable, inactive acid—meso-tartaric acid.

The question as to whether No. I represents *d*- or *l*-tartaric acid has been settled by *Fischer* (B. 1896, 29, 1377) in favour of the *d*-acid. We thus have:

1. **Dextro-tartaric acid**, *acidum tartaricum*, is the tartaric acid found in nature. It was discovered by *Scheele* in 1769. It occurs in the free state, but chiefly as acid potassium salt, in various fruits, especially in the juice of grapes, from which potassium hydrogen tartrate (cremor tartari) separates in crystals during fermentation. When this is boiled with chalk and chloride of calcium it is transformed into the neutral calcium salt, from which the acid is liberated on addition of H_2SO_4.

It crystallizes from water in large transparent monoclinic prisms, of a strong taste, is readily soluble in water, also in alcohol, but almost insoluble in ether. It melts at 170°, and its aqueous solution reduces a warm ammoniacal silver solution. When melted, it changes into an amorphous modification, and then into an anhydride, and when heated more strongly it chars, producing a characteristic odour and yielding pyro-racemic and pyro-tartaric acids. Oxidation converts it either into dihydroxy-tartaric (p. 270) or tartronic acid, and then into carbonic acid. It is employed in medicine and dyeing, and for making effervescent drinks.

Normal potassium tartrate, $C_4H_4O_6K_2 + \frac{1}{2}H_2O$, forms monoclinic prisms easily soluble in water. **Acid potassium tartrate, tartar,** or cremor tartari, $C_4H_5O_6K$, small rhombic crystals of acid taste, sparingly soluble in water, is much used in dyeing, medicine, &c. Potassium sodium tartrate, **Rochelle** or **seignette salt**, $C_4H_4O_6KNa + 4H_2O$ (1672), forms magnificent rhombic prisms. **Calcium tartrate,** $C_4H_4O_6Ca + 4H_2O$, is a powder insoluble in water, but soluble in cold caustic-soda solution; on warming the solution it separates as a jelly, which redissolves upon cooling. **Potassium antimonyl-tartrate, tartar emetic,** $C_4H_4O_6(SbO)'K + \frac{1}{2}H_2O$ (see B. 15, 1540), is obtained by heating cream of tartar (cremor tartari) with antimony oxide and water. It crystallizes in rhombic efflorescent octahedra, readily soluble in water. It is poisonous and acts as an emetic, and is used as a mordant in dyeing.

Fehling's solution is a solution of cupric sulphate mixed with alkali and Rochelle salt, and is largely used as an oxidizing agent. Thus with various carbon compounds, such as formaldehyde, glucose, fructose, &c., it readily yields a precipitate of cuprous oxide.

The **diethyl ester** is a thick oil, while the **monoethyl ester** crystallizes in prisms. **Aceto-tartaric acid** and **amides** of tartaric acid are known, and also various anhydrides. As an alcohol, it forms with nitric acid a dinitric ester, the so-called **nitro-tartaric acid,** $C_2H_2(O \cdot NO_2)_2(CO_2H)_2$, which is readily hydrolysed, yielding dihydroxy-tartaric or tartronic acid.

2. **Lævo-tartaric acid** is identical in its chemical and also in almost all its physical properties with ordinary tartaric acid, but differs from it in that its solutions turn the plane of polarization of light to the left, in a degree equal to that in which the other turns it to the right. The crystallized salts show hemihedral faces like the salts of dextro-tartaric acid, but oppositely situated (see p. 263). When equal quantities of both acids are mixed together in aqueous solution, the solution becomes warm, and we obtain:

3. **Racemic acid,** $(C_4H_6O_6)_2$, $2H_2O$, the composition of which was first established by *Berzelius*, who recognized it as being different from tartaric acid, and who developed the idea of isomerism from this first example in 1829. Racemic acid is obtained from tartar mother liquor. It differs from dextro-tartaric acid in that its crystals are rhombic and efflorescent, and also less soluble in water than the former; further, the free acid is capable of precipitating a solution of calcium chloride

and is optically inactive (see below). The salts, which are termed racemates, and also the esters (B. **21**, 518), show small differences from the tartrates in the proportions of their water of crystallization, in solubility, and melting-point or boiling-point. Molecular-weight determinations of dilute aqueous solutions of racemic acid indicate that under these conditions it is completely resolved into *d*- and *l*-tartaric acids.

4. **Meso-tartaric acid**, a fourth tartaric acid, is inactive like the foregoing, but non-resolvable into the active acids. When heated with water at 170° it is partially transformed into racemic acid, which can then be resolved. It differs from racemic acid and also from the active acids in all its physical properties. It crystallizes in efflorescent rectangular plates, m.-pt. 143°. The acid-potassium salt is readily soluble in water.

Racemic Compounds. *Resolution of Racemic Compounds into their Optically Active Components.*—Racemic acid has been resolved by three distinct methods, all due to *Pasteur*; and as they are also applicable to the resolution of other racemic compounds, they are given below.

1. When a solution of sodium-ammonium racemate,

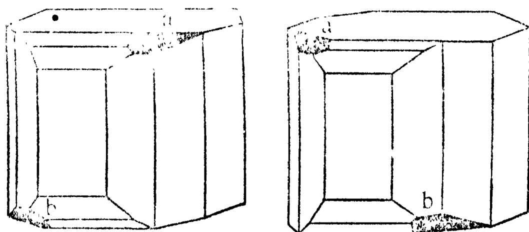


$$Na(NH_4)C_4H_4O_6,\ 2H_2O,$$

is evaporated, beautiful rhombic crystals having the composition $NaNH_4C_4H_4O_6,\ 4H_2O$ and showing hemihedral faces*

* *Hemihedral Faces.*—These are small faces which are not perfectly symmetrically situated with respect to the other crystalline faces; they occur in only half the positions where they might be expected, and thus give the crystals a non-symmetric structure.

The following figs. represent crystals of the *d*- and *l*-sodium ammonium tartrates:

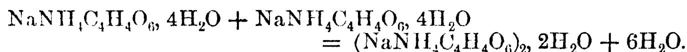


The faces *a* and *b* are the hemihedral faces, and it will be noticed that the two crystals are non-superposable, but stand in the relationship of object to mirror-image.

are obtained. *Pasteur* observed that these faces were not always similarly situated, but that certain crystals were dextro-hemihedral, while others were lævo-hemihedral, so that one crystal formed the reflected image of the other. The lævo-hemihedral crystals when dissolved exhibit dextro-rotation and *vice versa*. If now the two kinds of crystals be separated mechanically, and the free acid liberated from each, this will be found to consist, not of racemic acid, but in the one case of *d*- and in the other of *l*-tartaric acid.

In the process of crystallization it is essential that the temperature should be below 27°, as otherwise in place of the enantiomorphously related crystals of sodium-ammonium *d*- and *l*-tartrates, it is found that the crystals are all alike, possess no hemihedral faces, and consist of sodium-ammonium racemate. This temperature is termed the transition point, and for each racemic compound there is a definite transition temperature. Thus for sodium-potassium racemate it is 3°, for rubidium racemate 40·4°, for ammonium-hydrogen malate 74°.

The transition temperature may be determined by means of a dilatometer (*Van't Hoff* and *Deventer*, Zeit. Phys., 1887, **1**, 173). This is a large thermometer, the bulb of which is filled with an equimolecular mixture of the two active salts covered with oil, the level of which can be read off on the stem. As the temperature of the dilatometer is raised gradually, a considerable increase in volume is noticed at 27°, due to the change:



$$NaNH_4C_4H_4O_6, 4H_2O + NaNH_4C_4H_4O_6, 4H_2O = (NaNH_4C_4H_4O_6)_2, 2H_2O + 6H_2O.$$

Other racemic compounds have been resolved by this simple method of crystallization. In all cases the temperature employed must be below the transition temperature of the given substance, *i.e.* below the temperature at which the mixture of active components becomes transformed into the racemic compound. In this method of resolution no differences in solubility of the two components are met with, and hence no process of fractional crystallization can be employed; the two salts are deposited side by side, and must be picked out individually. The resolution of zinc ammonium lactate has already been mentioned (p. 223); further examples are sodium-potassium racemate, asparagin, and camphoric acid.

If crystallization occurs in the presence of an optically active solvent, *e.g.* solution of *l*-malic acid then a partial separation of antipodes may occur, cf. *M'Kenzie* and *Walker* (J. C. S., 1922, 349).

2. A very common method of resolving racemic acids is by combination with an optically active base, *e.g.* an alkaloid. In the case of racemic acid itself, *Pasteur* used *l*-cinchonine. The two salts formed are (*a*) *d*-acid + *l*-base, (*b*) *l*-acid + *l*-base. As these two salts are not enantiomorphously related, *i.e.* their molecules do not stand in the relationship of object to mirror-image, they possess different solubilities, and may be separated by fractional crystallization.

The following is a list of some simple racemic compounds which have been resolved by this method; the salt named is the less soluble of the two, and crystallizes first.

Acids.—Quinine: *d*-tartrate. Strychnine: *l*-lactate, *d*-methyl-succinate, *d*-methoxy-succinate, *d*-phenyldibromo-propionate. Cinchonine: *l*-tartrate, *d*-malate, *d*-mandelate. Brucine: *d*-tartrate, *l*-valerate, *l*-aspartate.

Racemic bases may be resolved by a similar process, viz. by combination with an optically active acid, *e.g.* *d*-tartaric, or even better, *d*-bromocamphor-sulphonic acid, and separating the two salts thus obtained by fractional crystallization. Thus ethyl-piperidine and coniine have been resolved by *Ladenburg* by using *d*-tartaric acid (A. 1888, **247**, 85; cf. also *Pope* and *Harvey* on resolution of tetrahydro-β-naphthylamine, J. C. S. 1901, 74; also *Pope* and *Peachey*, *ibid.* 1899, 1066 and 1105).

3. The third method consists in subjecting a solution of an ammonium salt of the acid to the action of some of the lower plant organisms, *e.g.* moulds, bacteria, yeasts, &c. Different organisms are required in different cases. *Pasteur* found that ordinary green mould—*Penicillium glaucum*—when grown in a solution of ammonium racemate, destroys the salt of the *d*-acid and leaves a solution of the salt of the *l*-acid. If, however, the decomposition is allowed to proceed, the *l*-salt is also destroyed; the reaction is a preferential decomposition, and, if stopped at a suitable time, practically all *d*-salt will have disappeared. It is obvious that in this method one of the active components is lost; but by using two distinct organisms in separate solutions it is sometimes possible to obtain both *d*- and *l*-compounds. Thus *Penicillium glaucum* grown in a solution of a salt of *d l*-mandelic acid leaves the *d*-salt, and *Saccharomyces ellipsoideus* leaves the *l*-salt.

Among other resolutions which have been effected by this method may be mentioned the destruction of *l*-lactic, *l*-mandelic, *d*-glyceric, *l*-ethoxy-succinic acids, and of *d*-methylpropyl-carbinol by *Penicillium glaucum*, and the destruction of *d*-mandelic,

l-phenyldibromo-propionic acids and of *d*-glucose, *d*-fructose, and *d*-mannose by yeast (different species).

4. *Markwald* and *M'Kenzie* (B. 1901, **34**, 469) have suggested another method of resolution, viz. by esterifying the racemic acid with an optically active alcohol. They used *r*-mandelic acid and *l*-menthol, and found that the *d*-component of the racemic acid was esterified somewhat more rapidly than the *l*. (Cf. also *Mackenzie*, J. C. S. 1904, 378.)

Wren and *Wright* (J. C. S. 1921, 798) find that the mixture of esters derived from *dl*-α-hydroxy- β-phenylpropionic acid and *l*-menthol when crystallized from light petroleum yields the *l*-menthyl ester of the *d*-acid in well defined crystals, and on hydrolysis this gives the *d*-acid.

5. *Ostromisslensky* (B. 1908, **41**, 3035) has shown that a mixture of *d*- and *l*-isomerides can be easily separated if a supersaturated solution of the mixture is impregnated with a crystal of a suitable active material, thus a crystal of *l*-asparagine (p. 257) immediately produces the deposition of *d*-sodium ammonium tartrate from a supersaturated solution containing the *d*- and *l*-salts. It is not necessary that the impregnating substance should be optically active; it must, however, be isomorphous or isodimorphous. Thus a crystal of glycine can cause the deposition of *l*-asparagine from a supersaturated solution of *d*-*l* asparagine. This method of resolution cannot be used when the supersaturated solution contains a definite racemic compound of the *d*-*l* isomerides, and can thus be used as a method for determining whether the given substance exists in solution as a *d*-*l* conglomerate or as a true racemic compound.

M'Kenzie and *Walker* (J. C. S. 1922, 349) find that certain racemates crystallized from aqueous solutions of *l*-malic acid yield a mixture of the racemate and *d*-tartrate.

Racemisation.—When *d*-tartaric acid is heated with a small amount of water at 175° racemic acid and a little meso acid are formed. This conversion of a *d*- or *l*- compound into its racemic isomeride is termed *racemisation*, and is due to the transformation of 50 per cent of the original active acid into its optical isomer. Other examples of racemisation are (*a*) the heating of *d*-valeric acid with concentrated sulphuric acid, (*b*) of amyl alcohol with sodium hydroxide. (*c*) Valeric acid boiled for eighty hours is partially racemised, as is indicated by a slight diminution in its rotatory power. Racemisation often occurs during a chemical reaction; thus *l*-mandelic acid, $C_6H_5 \cdot CH(OH) \cdot CO_2H$, and hydrobromic acid at 50° yield not *l*-phenylbromo-acetic but

r-phenylbromo-aceticacid. (Cf. also *Easterfield*, J. C. S. 1891, 72; *Pope*, *ibid.* 1901, 81; *James* and *Jones*, *ibid.* 1912, **101**, 1158.

For racemization during hydrolysis of esters with alcoholic potash, cf. J. C. S. 1919, **115**, 602, and Chap. XLVII, H.

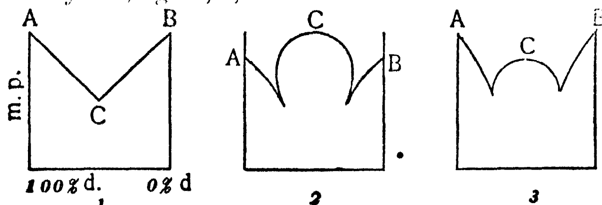
Occasionally the racemisation occurs at the ordinary temperature, and is then termed *autoracemisation*; thus *d*-phenylbromo-acetic acid when kept in benzene solution for some three years becomes quite inactive, and ethyl *d*-bromo-succinate in the course of four years diminishes in rotatory power from +40·96° to +9° (*Walden*, B. 1898, **31**, 1416).

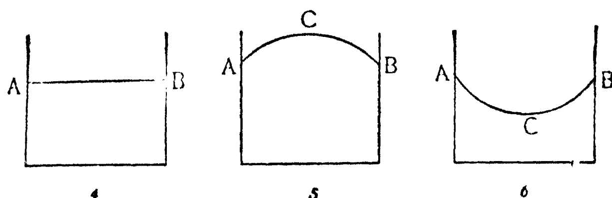
Criteria for Determining the Nature of the Racemic Compound.—The racemic substance may be one of the following:—(*a*) A definite compound of 1 molecule of the *d*-component with 1 of the *l*. (*b*) An ordinary mixture of the two in molecular proportions. (*c*) Mixed crystals, *i.e.* a solid solution of the two isomorphous antipodes without chemical combination. The first are termed racemic compounds proper, the second inactive conglomerates, and the third pseudoracemic compounds (*Kipping* and *Pope*, J. C. S. 1897, 989).

A true racemic compound cannot be recognized by molecular-weight determinations, as in the gaseous form or in solution it is usually resolved into its components. In certain cases the recognition of the substance as a racemic compound is simple, *e.g.* sodium-ammonium racemate, which crystallizes in a different crystallographic system, and contains a different amount of water of crystallization from the active isomers, and possesses a definite transition point.

When such simple criteria are of no use, *Backhuis Roozeboom* (Zeit. Phys. 1899, **28**, 494) recommends a study of the melting-point curves. These are obtained by taking the melting-points of mixtures of the compounds in different proportions, and then plotting the melting-points against the composition. The following types of curves are met with:—

Conglomerates, fig. 1. Racemic compounds, figs. 2 and 3. Mixed crystals, figs. 4, 5, and 6.





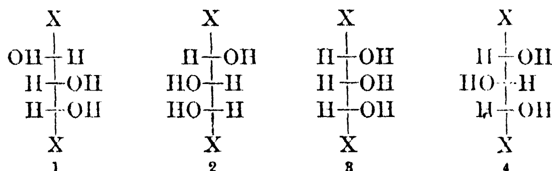
A represents the melting-point of the pure *d*-compound, B that of the pure *l*, and C that of the racemic compound or mixture. These curves should be studied by aid of the Phase rule.

E. Polyhydroxy Dibasic Acids

Trihydroxy-glutaric acid, $CO_2H \cdot CH(OH) \cdot CH(OH) \cdot CH(OH) \cdot CO_2H$, and the stereo-isomeric acids—saccharic, mucic, and isosaccharic acid—$CO_2H \cdot CH(OH) \cdot CH(OH) \cdot CH(OH) \cdot CH(OH) \cdot CO_2H$, are the best-known examples.

Many of these acids form lactones (p. 225), the so-called lactonic acids, and some of them also double lactones (cf. *Fittig*, A. 255, 1, *et seq.*).

Trihydroxy-glutaric acid, $CO_2H \cdot (CH \cdot OH)_3 \cdot CO_2H$, is a frequent oxidation-product of sugar varieties, *e.g.* of xylose and arabinose. According to theory, four stereo-isomers should exist, and four are actually known; they may be represented by the following projection formulæ, where $X = CO_2H$:—



Nos. 1 and 2 are enantiomorphously related and optically active, and can form a racemic compound. Compounds 3 and 4 are inactive substances of the type of mesotartaric acid.

Saccharic acid is produced by the oxidation of cane-sugar, glucose, gulose, gulonic acid, mannitol, or starch by nitric acid, and exists in the *d*-, *l*-, and *r*-forms (see Glucoses); *d*-saccharic acid when reduced yields glycuronic acid (see p. 230). All the three varieties are deliquescent.

Mucic acid is formed by oxidizing dulcitol, the gums, muci-

lages, and milk-sugar. It is a sparingly soluble, colourless, crystalline powder. The molecule being symmetrical in structure, it is optically inactive. It is easily converted into derivatives of furane (Chap. XXXIV).

Isosaccharic acid is obtained by the oxidation of glucosamine, $C_6H_{11}O_5(NH_2)$.

Theoretically, ten stereo-isomeric acids of the formula $CO_2H \cdot [CH \cdot OH]_4 \cdot CO_2H$ are possible, most of which (*e.g.* **d- and i-manno-saccharic acids, talomucic acid**, &c.) have been prepared by *E. Fischer* (B. **24**, 539, 2137, 3622). For their relations to the hexoses, see the table appended to these.

F. Dibasic Ketonic Acids

Dibasic ketonic acids unite in themselves the properties of a ketone and of a dibasic acid. The following are known:—

1. **Mesoxalic acid**, $CO(CO_2H)_2$ or $C(OH)_2(CO_2H)_2$ (see p. 206), is prepared from dibromo-malonic acid, $CBr_2(CO_2H)_2$, and baryta water or oxide of silver, thus:—



$$CBr_2(CO_2H)_2 + H_2O = CO(CO_2H)_2 + 2HBr;$$

also by boiling alloxan (p. 298) with baryta water. It crystallizes in deliquescent prisms $(+H_2O)$.

As a ketone it combines with $NaHSO_3$, reacts with hydroxylamine, and is reduced by nascent hydrogen to tartronic acid:



$$CO_2H \cdot CO \cdot CO_2H + 2H = CO_2H \cdot CH(OH) \cdot CO_2H.$$

Since the acid and its salts still retain a molecule of water at temperatures above 100°, this may be united in much the same manner as the water in chloral hydrate, corresponding with the formula $C(OH)_2(CO_2H)_2$, "dihydroxy-malonic acid". In fact, two modifications of the ethyl ester are known, viz. $C(OH)_2(CO_2C_2H_5)_2$ and $CO(CO_2C_2H_5)_2$.

2. **Oxal-acetic acid**, *Butanone diacid*, $CO_2H \cdot CH_2 \cdot CO \cdot CO_2H$, is an acid corresponding in many respects with aceto-acetic acid. Its **ethyl ester** is prepared by the action of sodium ethoxide upon a mixture of ethyl oxalate and acetate (p. 232), and also by the action of concentrated sulphuric acid upon ethyl acetylene-dicarboxylate. It is a colourless oil, but the alcoholic solution gives an intense dark-red coloration with ferric chloride. It is of importance as a synthetical reagent, as the hydrogen atoms of the methylene group can be replaced by

sodium, and hence by various alkyl and acyl radicals (*W Wislicenus*).

3. **Acetone-dicarboxylic acid**, *Pentanone diacid*, $CO(CH_2 \cdot CO_2H)_2$, obtained by treating citric acid with concentrated H_2SO_4, readily decomposes into acetone and $2CO_2$ (see A. **261**, 151).

4. **Dihydroxy-tartaric acid**, $CO_2H \cdot CO \cdot CO \cdot CO_2H$, or probably $CO_2H \cdot C(OH)_2 \cdot C(OH)_2 \cdot CO_2H$, is formed from pyrocatechol and nitrous acid, and by the gradual decomposition of nitro-tartaric acid. It melts at 98°. The characteristic sparingly soluble sodium salt decomposes readily into carbon dioxide and sodium tartronate.

5. **Diaceto-succinic acid**, $\begin{matrix} CH_3 \cdot CO \cdot CH \cdot CO_2H \\ CH_3 \cdot CO \cdot \dot{C}H \cdot CO_2H \end{matrix}$ (see p. 237).
The ester of this is closely related to acetonyl-acetone, the latter being readily obtainable from the former by the action of caustic-soda solution ("Ketonic decomposition"; cf. B. **33**, 1219).

6. **Diacetoglutaric acid**, $CO_2H \cdot CHAc \cdot CH_2 \cdot CHAc \cdot CO_2H$. The ester of this acid is formed by condensing ethyl acetoacetate with formaldehyde in the presence of diethylamine, and is readily converted into derivatives of tetrahydrobenzene or pyridine (*Knoevenagel*, A. **281**, 94; cf. also B. **31**, 1388).

Most of these ketonic acids exhibit keto-enolic tautomerism, thus 5 isomerides of diacetyl-succinic acid are known (*Knorr* A. 1899, **306**, 332. Cf. Chap. XLVII, G.)

XI. POLYBASIC ACIDS

The polybasic acids contain two or more carboxylic groups in the molecule. The tribasic acids, like phosphoric acid, can give rise to three series of salts—normal, monoacid, and diacid. Both saturated and unsaturated acids are known, and also substituted derivatives.

A. Saturated and Unsaturated Polybasic Acids

A simple tribasic acid is **tricarballylic acid**, *symmetrical propane-tricarboxylic acid*, $CO_2H \cdot CH_2 \cdot CH(CO_2H) \cdot CH_2 \cdot CO_2H$. It occurs in unripe beet, and is prepared (*a*) by the addition of hydrogen to aconitic acid, (*b*) by heating citric acid with hydriodic acid, and (*c*) synthetically from glycerol by transforming it into the tribromhydrin, $C_3H_5Br_3$, treating this with

KCN, and hydrolysing the cyanide formed, $C_3H_5(CN)_3$. Since the three hydroxyls in glycerol are distributed among three carbon atoms, the same holds good for the carboxyls in the acid, which has, therefore, the symmetrical constitution:



$$CO_2H \cdot CH_2 \cdot CH(CO_2H) \cdot CH_2 \cdot CO_2H.$$

This acid is of importance in determining the constitution of citric acid, from which, as already seen, it can be obtained by reduction with HI. It crystallizes in rhombic prisms, is readily soluble in water, and melts at 166°.

An unsaturated tribasic acid closely related to tricarballylic acid is **aconitic acid**, $CO_2H \cdot CH{:}C(CO_2H) \cdot CH_2 \cdot CO_2H$, which contains two atoms of hydrogen less than tricarballylic acid. It is found in nature, in *Aconitum Napellus*, shave-grass, sugar-cane, beet-root, &c., and is prepared by heating citric acid, $C_6H_8O_7$, when the elements of water are eliminated. It is a strong acid, crystallizable, readily soluble in water, melts at 191°, and is reduced by nascent hydrogen to tricarballylic acid, hence its constitution.

B. Hydroxy Polybasic Acids

Citric acid, *acidum citricum, hydroxy-tricarballylic acid*, $CO_2H \cdot CH_2 \cdot C(OH)(CO_2H) \cdot CH_2 \cdot CO_2H$ (*Scheele*, 1784; recognized as tribasic by *Liebig* in 1838), occurs in the free state in lemons, oranges, and red bilberries, and mixed with malic acid in gooseberries, &c., also as calcium salt in woad, potatoes, beet-root, &c. It is usually prepared from the juice of lemons by means of the lime salt. It crystallizes in large rhombic prisms ($+ H_2O$), is readily soluble in water, moderately in alcohol, but only sparingly in ether. It loses its water of crystallization at 130°, melts at 153°, and breaks up at a higher temperature first into aconitic acid and water, and then into carbon dioxide, itaconic acid, citraconic anhydride, and acetone. Oxidizing agents effect a very thorough decomposition.

Calcium citrate is precipitated as a white sandy powder when a mixture of calcium chloride and alkali citrate solutions is boiled. The three series of salts are well characterized; the alkali salts are soluble in water, the others mostly insoluble. Among the derivatives may be mentioned **mono-, di-**, and **tri-ethyl citrates** and **triethyl aceto-citrate**,



$$CO_2Et \cdot CH_2 \cdot C(O \cdot CO \cdot CH_3)(CO_2Et) \cdot CH_2 \cdot CO_2Et.$$

The formation of this last is a direct proof of the alcoholic character of citric acid. The **amides** of citric acid are converted by concentrated H_2SO_4 into **citrazinic acid**, $C_6H_5NO_4$, a pyridine derivative (B. **17**, 2681).

The *constitution* of citric acid is arrived at (*a*) from its conversion into aconitic acid by the elimination of water, (*b*) from its reduction to tricarballylic acid, and (*c*) from its synthesis from 1 : 3 dichloroacetone, *e.g.*:

$$CH_2Cl\cdot CO\cdot CH_2Cl + HCN \rightarrow CH_2Cl\cdot C(OH)(CN)\cdot CH_2Cl$$
$$\rightarrow CN\cdot CH_2\cdot C(OH)(CN)\cdot CH_2\cdot CN$$
$$\rightarrow CO_2H\cdot CH_2\cdot C(OH)(CO_2H)\cdot CH_2\cdot CO_2H.$$

The acid has been synthesised by *Lawrence* (J. C. S. 1897, 71, 457) by an application of *Reformatsky's* reaction, *i.e.* the condensation of a halogen derivative with a ketone in the presence of zinc (cf. p. 128). The substances used were ethyl bromacetate, ethyl oxalacetate, and pure zinc turnings:

$$CO_2Et\cdot CH_2Br + \begin{matrix} CO\cdot CO_2Et \\ \dot{C}H_2\cdot CO_2Et \end{matrix} + Zn = \begin{matrix} CO_2Et\cdot CH_2\cdot C(OZnBr)\cdot CO_2Et \\ \dot{C}H_2\cdot CO_2Et. \end{matrix}$$

This condensation product reacts with water, yielding ethyl citrate, $CO_2Et\cdot CH_2\cdot C(OH)(CO_2Et)\cdot CH_2\cdot CO_2Et$, zinc oxide, and hydrogen bromide.

Citric acid is also formed when solutions of glucose are fermented by certain moulds, *e.g. Citromycetes pfefferianus* and *C. glaber* (*Wehner*, Bull. Soc. Chim. 1893 [III], **9**, 728).

Acids containing more than three carboxylic groups do not, as a rule, occur in nature, but a number of esters of such acids have been prepared by means of the aceto-acetic ester and malonic ester syntheses.

XII. CYANOGEN COMPOUNDS

Under the name of the cyanogen compounds is included a group of substances which are derivable from cyanogen, C_2N_2. Cyanogen itself is a gas of excessively poisonous properties which behaves in many respects like a halogen; and its hydrogen compound, **hydrocyanic acid**, HCN, is an acid re-

sembling hydrochloric acid to a certain extent. In many cyanogen compounds the monovalent group (CN) plays the part of an element; cyanogen is to be regarded as the isolated radical (CN), which, however, possesses the double formula C_2N_2, just as a molecule of chlorine (Cl_2) is made up of two atoms. The cyanogen group is further capable of combining with the halogens, hydroxyl, sulphydril (SH), amidogen, &c. From the compounds so obtained numerous others are derived by the entrance of alkyl radicals in place of hydrogen. Such derivatives invariably exist in two isomeric forms, sharply distinguished from one another by their properties. They are often termed normal and iso compounds, and the isomerism is of very great interest. (See table, p. 274.)

Polymeric modifications of most of those compounds also exist. The number of cyanogen compounds known is thus a very large one.

Carbon and nitrogen do not combine directly except in the presence of an alkali, and then a metallic cyanide is formed. As examples of this reaction, we have the following:—

1. When nitrogen is led over a red-hot mixture of coal and carbonate of potash, potassium cyanide, KCN, is formed, especially under a high pressure.

2. Ammonium cyanide is formed when ammonia is passed over red-hot coal.

3. Potassium cyanide is formed when nitrogenous organic compounds such as leather, horn, claws, wool, blood, &c., are heated with potashes.

4. Hydrocyanic acid is formed when electric sparks are passed through a mixture of acetylene and nitrogen, and also by the action of the silent electric discharge on a mixture of cyanogen and hydrogen. It is also formed (commercial method) when a carefully dried mixture of hydrogen, ammonia, and a volatile carbon compound (CO, CO_2, C_2H_2, &c.) is passed over heated platinized pumice. (For further modes of formation, see p. 275 *et seq.*)

The original material for the preparation of most of the cyanogen compounds is potassium ferrocyanide, which is manufactured on the large scale and possesses the great advantage over potassium cyanide of being stable in the air and comparatively non-poisonous.

SUMMARY OF THE CYANOGEN COMPOUNDS

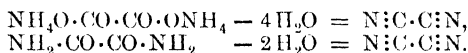
Relation to carbonic acid, &c. (See p. 288.)	Name.	Formula.
Nitrile of oxalic acid,	*Cyanogen,*	N⁝C·C⁝N
Nitrile of formic acid,	*Hydrocyanic acid,* Alkyl derivatives: (*a*) Nitriles, (*b*) Isonitriles,	N⁝C·H R·C⁝N R·N:C
	Cyanogen chloride, bromide, iodide,	N⁝C·Cl
$CO_3H_2 + NH_3 - 2H_2O$, (Nitrile of carbonic acid, eventually Carbimide),	*Cyanic acid,* Alkyl derivatives: (*a*) Methyl cyanate, (*b*) „ isocyanate,	N⁝C·OH N⁝C·O·CH_3 O:C:N·CH_3
	Thiocyanic acid, Alkyl derivatives: (*a*) Ethyl thiocyanate, (*b*) Allyl isothiocyanate,	N⁝C·SH N⁝C·S·C_2H_5 S:C:NC_3H_5
$CO_3H_2 + 2NH_3 - 3H_2O$, (Nitrile and amide of carbonic acid, eventually Carbo-di-imide, see p. 286),	*Cyanamide,* Alkyl derivatives: (*a*) Alkyl cyanamide, (*b*) Carbo-di-imide,	N⁝C·NH_2 N⁝C·NH·R RN:C:NR*
The amic acid of carbonic acid,	*Carbamic acid,*	NH_2·CO·OH
The amide of carbonic acid,	*Urea,*	$CO(NH_2)_2$
	Thio-urea, Alkyl derivatives: (*a*) Alkyl-thio-ureas, (*b*) Imido-thio-carbamine compounds,	$CS(NH_2)_2$ NH_2·CS·NHR NH:C<(NH_2)(SR)
$CO_3H_2 + 3NH_3 - 3H_2O$, (Amidine),	*Guanidine,*	$HN:C(NH_2)_2$

* R = alkyl radical.

A. Cyanogen and Hydrocyanic Acid

Cyanogen, $N{:}C{\cdot}C{:}N$, which was discovered by *Gay-Lussac* **in 1815,** occurs in the gases of blast-furnaces and in coal gas.

As the nitrile of oxalic acid, it may be obtained by the abstraction of the elements of water from ammonium oxalate by means of P_4O_{10}; also in the same way from the intermediate product of this reaction, oxamide:



$$NH_4O{\cdot}CO{\cdot}CO{\cdot}ONH_4 - 4\,H_2O = N{:}C{\cdot}C{:}N,$$
$$NH_2{\cdot}CO{\cdot}CO{\cdot}NH_2 - 2\,H_2O = N{:}C{\cdot}C{:}N.$$

It is usually prepared by heating dry silver cyanide, AgCN, or mercuric cyanide, $Hg(CN)_2$, strongly:



$$Hg(CN)_2 = Hg + C_2N_2;$$

or by heating a solution of cupric sulphate with potassium cyanide (B. 18, Ref. 321).

Cyanogen is a colourless gas of a peculiar unpleasant odour resembling that of bitter almonds, and is terribly poisonous. It is easily liquefied and solidified (sp. gr. 1·8 of the liquid; m.-pt. −34°; b.-pt. −21°), is soluble in 0·25 vol. of water and in even less alcohol. The solutions become dark upon standing, with separation of a brown powder ("Azulmic acid"), while oxalic acid, ammonia, formic acid, hydrocyanic acid, and urea are to be found in the liquid. The formation of the oxalic acid and ammonia is due to normal hydrolysis, and that of formic acid to the hydrolysis of the hydrocyanic acid formed as an intermediate product. In presence of a minute quantity of aldehyde, oxamide is formed as the result of the addition of water. Cyanogen combines with heated potassium to KCN, and dissolves in aqueous potash to form KCN and KCNO.

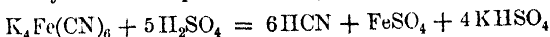
Paracyanogen, $(CN)_x$, is a polymer of cyanogen. It is an amorphous brown powder which is formed as a by-product when mercuric cyanide is heated; upon further heating, it is transformed into cyanogen.

Hydrocyanic acid, *prussic acid*, CNH, was discovered about the year 1782 by *Scheele*, and investigated closely by *Gay-Lussac.*

Some of the more interesting methods of formation are the following:—

1. It is readily liberated from its salts by the action of **almost any other acid, even carbonic acid; and even complex**

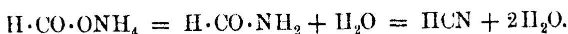
cyanides, *e.g.* potassium ferrocyanide, when distilled with moderately dilute sulphuric acid yield hydrogen cyanide:



$$K_4Fe(CN)_6 + 5H_2SO_4 = 6HCN + FeSO_4 + 4KHSO_4$$

The ferrous sulphate produced reacts with more ferrocyanide to form potassium ferrous ferrocyanide, $FeK_2(FeC_6N_6)$, which is not affected by dilute acids (see p. 279); consequently only half of the cyanogen present is converted into hydrocyanic acid. When concentrated sulphuric acid is employed, carbon monoxide is obtained from the intermediate product, formic acid.

2. As the nitrile of formic acid, it may be prepared by the action of dehydrating agents on ammonium formate or formamide:



$$H \cdot CO \cdot ONH_4 = H \cdot CO \cdot NH_2 + H_2O = HCN + 2H_2O.$$

3. Together with oil of bitter almonds, $C_6H_5 \cdot CHO$, and grape-sugar, $C_6H_{12}O_6$, by the hydrolysis of the glucoside amygdalin under the influence of the enzyme "emulsin" (see Benzaldehyde, Chap. XXV, B.):



$$C_{20}H_{27}O_{11}N + 2H_2O = CNH + C_7H_6O + 2C_6H_{12}O_6$$

The oil of bitter almonds and its aqueous solution (*aqua amarum amygdalarum*)—prepared from the almonds themselves—consequently contain HCN.

The acid occurs in the free state in the tree *Pangium edule*, found in Java, more particularly in the seeds. It exists in the form of glucosides in various plants (C. C. 1906, ii, 1849; 1909, i, 387), which are termed cyanogenetic plants.

4. By the action of ammonia and chloroform on alcoholic potash under pressure. Cf. p. 106.

For other syntheses, see p. 273.

Hydrogen cyanide is a colourless liquid boiling at 26° and solidifying at −14°. Sp. gr. 0·70. It has a peculiar odour and produces an unpleasant irritation in the throat, is miscible with water, and burns with a violet flame. Like potassium cyanide, it is one of the most terrible of poisons. The best antidotes are stated to be hydrogen peroxide or small quantities of chlorine mixed with air. When absolutely pure it can be preserved unchanged, but it decomposes in presence of traces of water or ammonia, with separation of a brown mass and formation of ammonia, formic acid, oxalic acid, &c. The addition of minute quantities of mineral acids renders the aqueous solution more stable.

Liquid hydrocyanic acid is a good solvent for many salts, and has a high ionizing power. Acids (sulphuric and trichloroacetic), however, do not appear to dissociate when dissolved in the liquid.

The acid has many properties of an unsaturated compound. It is readily reduced by nascent hydrogen to methylamine. In the presence of hydrochloric acid it combines with water yielding formamide. With diazomethane (Chap. LI) it yields methyl cyanide together with methyl carbylamine. With hydrogen chloride it gives *iminoformyl chloride*, NH:CHCl, a compound of importance in the synthesis of aromatic aldehydes (A. 1906, **347**, 347); but has not been isolated. From ethyl acetate solution a product 2HCN, 3HCl = NH:CH·NH·$CHCl_2$, HCl, dichloromethyl formamidine hydrochloride is obtained. It combines directly with most aldehydes and ketones, yielding cyanhydrins (nitriles of hydroxy acids), (p. 214), and also with certain unsaturated compounds, especially in the presence of potassium cyanide, yielding saturated nitriles (*Lapworth*, J. C. S. 1903, 995; 1904, 1214; *Knoevenagel*, B. 1904, **37**, 4065); *e.g.* α-phenylcinnamo-nitrile, CHPh:CPh·CN, yields diphenylsuccinylo-nitrile, CN·CHPh·CHPh·CN.

Hydrocyanic acid is an extremely weak monobasic acid ($K = 0{\cdot}0013 \times 10^{-6}$), and its salts are decomposed even by carbonic acid. It is a typical tautomeric compound. Its reduction to an amine and its hydrolysis to formic acid are similar to the corresponding reactions of methyl cyanide, and it might be urged that these reactions favour the nitrile formula H·C⋮N Both reactions are, however, compatible with the view that it has the carbylamine structure H·N:C. The salts are usually regarded as carbylamine derivatives (see derivatives of divalent carbon, Chap. L, E. 2.), and it might be argued that the free acid has a similar structure. Such an argument is, however, unsound, as numerous examples are known where salts have a structure quite different from that of the acid from which they are prepared (cf. ethyl acetoacetate and pseudo acids).

Hydrocyanic acid can be detected by converting it either into Prussian blue or into ferric thiocyanate. In the former case the solution to be tested is treated with excess of caustic soda and some ferrous and ferric salt, boiled, and acidified, when Prussian blue results; in the latter the solution is evaporated to dryness together with a little yellow sulphide

of ammonium, the residue taken up with water and ferric chloride added, when the blood-red colour of ferric thiocyanate is obtained.

Trihydrocyanic acid, $(CNH)_x$, results from the polymerization of hydrocyanic acid under certain specified conditions. It forms white, acute-angled crystals, which readily yield hydrogen cyanide when heated above 180°.

Cyanides.—The cyanides of the alkali and alkali-earth metals are soluble in water, and the solutions have a strongly alkaline reaction due to the hydrolysing action of the water (cf. Soaps, p. 165). The salts of the heavy metals, with the exception of mercuric cyanide, are insoluble in water.

Potassium cyanide, KCN, forms colourless deliquescent cubes, sparingly soluble in alcohol. The commercial product usually contains large amounts of potassium carbonate due to the action of atmospheric carbon dioxide. It is formed when potassium ferrocyanide is fused, and the product extracted with water: $K_4FeC_6N_6 = 4\,KCN + FeC_2 + N_2$.

Manufacturing processes.—(*a*) *Beilby's* process, which consists in treating a fused mass of potassium carbonate and carbon with ammonia, the product being a molten cyanide of high strength. (*b*) The sodium salt required for extracting gold from auriferous quartz is made by fusing sodium ferrocyanide, a by-product of gas-works, with sodium $Na_4FeC_6N_6 + 2\,Na \longrightarrow 6\,NaCN + Fe$. (*McArthur-Forrest* process.)

The pure salt can be prepared by passing hydrogen cyanide into an alcoholic solution of potassium hydroxide. It reacts with hydrogen peroxide in two different ways (cf. *Masson*, J. C. S. 1907, 1449):

1. 80 % $KCN + H_2O_2 \longrightarrow KCNO + H_2O$ and
$KCNO + 2\,H_2O \longrightarrow NH_3 + KOH + CO_2$;
2. 20 % $KCN + 2\,H_2O \longrightarrow NH_3 + H \cdot COOK$.

Mercuric cyanide, $Hg(CN)_2$, crystallizes in colourless prisms, is stable in the air, readily soluble in water, and excessively poisonous. Its aqueous solution is a non-conductor of the electric current, and does not give the ordinary reactions for a mercuric salt or for a cyanide (cf. B. 1908, **41**, 317). **Argentic cyanide**, AgCN, forms a white flocculent precipitate closely resembling argentic chloride in appearance, but is soluble in hot concentrated nitric acid.

Complex Cyanides.—The double cyanides, which are produced by dissolving the insoluble metallic cyanides in a solution of potassium cyanide, are divided into two classes. The

members of the one class are decomposed again on the addition of dilute mineral acids, with separation of the insoluble cyanide and formation of hydrocyanic acid, *e.g.* $KAg(CN)_2$; $K_2Ni(CN)_4$. The gold and silver double salts are largely used in gold and silver electro-plating. The members of the other class are much more stable and do not evolve hydrocyanic acid; to this class belong **potassium ferrocyanide**, $K_4Fe(CN)_6$, [$Fe(CN)_2$, 4 KCN], and **potassium ferricyanide**, $K_3Fe(CN)_6$, [$Fe(CN)_3$, 3 KCN]. The members of this second class are often termed **complex salts**, and are the metallic salts of complex acids, *e.g.* **hydroferrocyanic acid**, $H_4FeC_6N_6$, and **hydroferricyanic acid**, $H_3FeC_6N_6$, which are formed when the salts are decomposed with mineral acids. Certain salts of the latter acid are not decomposed at all by dilute acids, for instance Prussian blue, but they are by caustic potash (which converts Prussian blue into $Fe(OH)_3$ and $K_4FeC_6N_6$).

These salts, as a rule, do not give the reactions of simple cyanides, *e.g.* white precipitate with silver-nitrate solution, since in solution they do not yield the simple cyanide ions $\overline{CN}$ but the more complex anions $\overline{FeC_6N_6}$ and $\overline{FeC_6N_6}$.

Potassium ferrocyanide, *yellow prussiate of potash*, $K_4Fe(CN)_6 + 3H_2O$, may be obtained by adding excess of potassium cyanide to a solution of ferrous sulphate, or by dissolving iron in a solution of cyanide of potassium, when hydrogen is evolved, thus:—



$$2KCN + Fe + 2H_2O = Fe(CN)_2 + 2KOH + H_2;$$
$$Fe(CN)_2 + 4KCN = K_4Fe(CN)_6.$$

The old commercial method consisted in fusing together scrap-iron, nitrogenous organic matter, and crude potassic carbonate.

It is now usually manufactured from the hydrogen cyanide present in crude coal gas or the gas from coke ovens. The spent oxide used in the purification of coal gas contains Prussian blue (ferric ferrocyanide, p. 280). The spent oxide is heated with hot milk of lime, and the Prussian blue thus transformed into calcium ferrocyanide, from which the potassium salt can be prepared.

Another method consists in passing the coal gas, before it has been subjected to dry purification, through an alkaline solution containing an iron salt. The sulphuretted hydrogen reacts with the iron salt, forming ferrous sulphide, and this

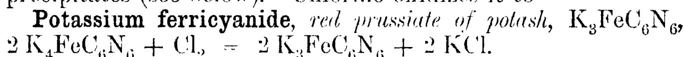
with the hydrogen cyanide and alkali (potassium carbonate) yields potassium ferrocyanide:



$$FeS + 6\,HCN + 2\,K_2CO_3 = K_4FeC_6N_6 + H_2S + 2\,CO_2 + 2\,H_2O.$$

It forms large, lemon-coloured monoclinic plates, which are stable in the air and easily soluble in water, but insoluble in alcohol. Concentrated HCl yields **hydro-ferrocyanic acid,** $H_4FeC_6N_6$, in the form of white needles. With a solution of $CuSO_4$, a red-brown precipitate of **cupric ferrocyanide,** or *Hatchett's* brown, $Cu_2FeC_6N_6$, is thrown down, and with solutions of ferrous and ferric salts the well-known characteristic precipitates (see below). Chlorine oxidizes it to

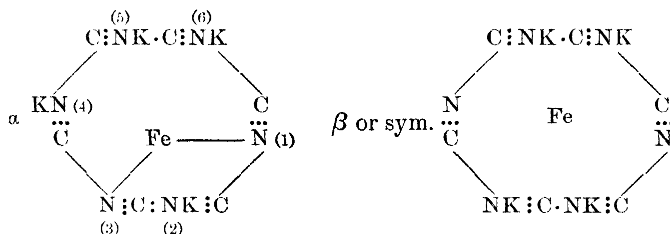
Potassium ferricyanide, *red prussiate of potash*, $K_3FeC_6N_6$,



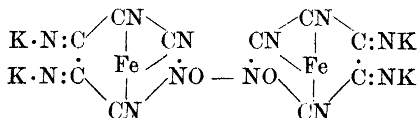
$$2\,K_4FeC_6N_6 + Cl_2 = 2\,K_3FeC_6N_6 + 2\,KCl.$$

This crystallizes in long, dark-red, monoclinic prisms which are readily soluble in water. The solution decomposes when kept, and acts as a strong oxidizing agent in the presence of alkali, potassium ferrocyanide being reproduced. **Hydro-ferricyanic acid,** $H_3FeC_6N_6$, forms unstable brown needles.

Both potassium ferri- and ferrocyanides exist in two isomeric forms, termed α and β (*Briggs*, J. C. S. 1911, **99**, 1019). The α is stable in alkaline solution but passes into the β in neutral or acid solvents. *Friend* (*ibid.* 1916, **109**, 715; cf. *Turner*, *ibid.* 1130) suggests the following formulæ for the α and β ferrocyanides:



It is the β-form which yields the nitro-prusside (p. 281), and as this exists in only one form is probably

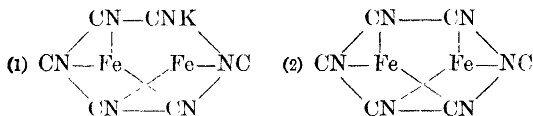


The α and β ferricyanides are represented by formulæ

similar to those for the ferrocyanides, except that the Fe radicle is tervalent and attached to nitrogen atoms 1:3:5 in the α and 1:2:4 in the β compound.

Ferrous salts with potassium ferrocyanide yield a white precipitate of dipotassium ferrous ferrocyanide, $K_2Fe(FeC_6N_6)$, which rapidly turns blue owing to the formation of potassium ferric ferrocyanide, soluble Prussian blue, $KFe(FeC_6N_6)$, which is formed by the interaction of ferric salts with an excess of $K_4FeC_6N_6$, or ferrous salts with an excess of $K_3FeC_6N_6$.

Insoluble Prussian blue (*Williamson's* blue) is formed by precipitating potassium ferricyanide with an excess of ferrous sulphate or the ferrocyanide with an excess of ferric chloride. (*Hofmann*, A. 1904, **337**, 1; cf. also *Deniges*, Bull. Soc. 1916, **19**, 79). The following formulæ for the soluble (1) and insoluble (2) Prussian blues are in harmony with the above facts:

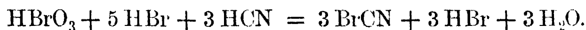


Sodium nitro-prusside, $Na_2FeC_5N_5(NO) + 2H_2O$, crystallizes in red prisms soluble in water, and yields a brilliant but transient violet coloration with alkali sulphides.

B. Halogen Compounds of Cyanogen

Cyanogen chloride, $Cl \cdot N:C$ (*Berthollet*), is a colourless gas with an obnoxious odour, and boils at 15·5°. It is prepared by the action of chlorine upon mercuric cyanide or upon dilute aqueous hydrocyanic acid, $CNH + Cl_2 = CNCl + HCl$. It polymerizes readily to cyanuric chloride, and yields sodium chloride and cyanate with aqueous sodium hydroxide.

Cyanogen bromide, CNBr, forms transparent prisms, and is prepared by the action of sulphuric acid on a mixture of bromate, bromide, and cyanide of sodium:



$$HBrO_3 + 5\,HBr + 3\,HCN = 3\,BrCN + 3\,HBr + 3\,H_2O.$$

Cyanogen iodide, CNI, forms beautiful white prisms, smelling intensely both of cyanogen and iodine, and subliming with the utmost ease. (Cf. *Chattaway* and *Wadmore*, J. C. S. 1902, 191.)

Cyanuric chloride, *trichlorocyanogen*, $(CCl)_3N_3$, is obtained from cyanogen chloride, or from hydrocyanic acid and chlorine in ethereal solution. It forms beautiful white crystals with an unpleasant odour, and has m.-p. 145° and b.-p. 190°.

For general discussion of urea, cyanic acid, cyamelide and cyanuric acid, cf. *Chattaway*, J. C. S. 1912, **101**, 170; *Werner*, 1913, **103**, 1010, 2275.

C. Cyanic and Cyanuric Acids

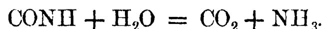
Cyanuric acid is formed when urea is heated, either alone or in a stream of chlorine gas; and when this acid is distilled, and the vapour condensed in a freezing-mixture, **cyanic acid**, CNOH, is obtained as a mobile liquid of a pungent odour:



$$C_3N_3O_3H_3 = 3CNOH$$

It is exceedingly unstable; when taken out of the freezing-mixture it changes, with explosive ebullition, into a white porcelain-like mass which consists of cyanuric acid 70 per cent, and cyamelide 30 per cent. **Potassium cyanate**, CNOK, frequently also termed potassium isocyanate, is prepared by the oxidation of an aqueous solution of potassium cyanide by means of permanganate (A. **259**, 377); or by fusing potassium cyanide or yellow prussiate of potash with PbO_2 or MnO_2: (CNK + O = CNOK). It crystallizes in white plates, readily soluble in water and alcohol. **Ammonium cyanate**, $CNO(NH_4)$, forms a white crystalline mass, and is of especial interest on account of the readiness with which it changes into the isomeric urea, $CO(NH_2)_2$ (p. 290).

When these salts are decomposed with mineral acids, free cyanic acid is not formed, but its products of hydrolysis, viz. carbon dioxide and ammonia:



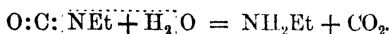
$$CONH + H_2O = CO_2 + NH_3.$$

This decomposition is avoided by the addition of dilute acetic acid (instead of hydrochloric), but in the latter case the cyanic acid changes into its polymer cyanuric acid, and the hydrogen-potassium salt of the latter slowly crystallizes out.

When the hydrogen atom in the cyanic acid molecule is replaced by alkyl radicals, two distinct groups of compounds are possible. The derivatives which are constituted on the type N:C·O·R are termed the *normal*, and those on the type O:C:N·R the *iso-compounds*.

Ethyl isocyanate, *cyanic ether*, $O:C:N\cdot CH_2\cdot CH_3$, obtained when potassium cyanate is distilled with ethyl iodide or potassium ethyl-sulphate, is a colourless liquid of suffocating odour, distilling at 60°, and is decomposed by water. It does

not behave as a typical ester, since when hydrolysed with acids or alkalis it yields ethylamine and carbon dioxide:



$$O:C:NEt + H_2O = NH_2Et + CO_2.$$

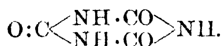
Water, which acts in a similar manner, gives rise to the more complicated urea derivatives; ammonia and amines also produce derivatives of urea, and alcohol yields derivatives of carbamic acid (see Carbonic Acid Derivatives).

The production of ethylamine as one of the products of hydrolysis is usually regarded as a strong argument in favour of the view that in the original isocyanate the ethyl group is attached to nitrogen and not to oxygen, *e.g.* O:C:N·Et. It is questionable, however, whether free cyanic acid and cyanate of potassium possess analogous constitutions, since frequent observations have shown that the normal cyanic compounds readily change into the iso- (see below); theoretical considerations indeed make it more probable that cyanic acid has the constitution N⋮C·OH, according to which it appears as the normal acid, with cyanogen chloride as its chloride.

Normal cyanic esters are not known (cf. A. **287**, 310).

Cyanuric acid, $C_3N_3O_3H_3$, $= (CN)_3(OH)_3$ (*Scheele*), obtained by heating urea, or by the action of water on cyanuric chloride, forms transparent prisms containing two molecules of water of crystallization. It effloresces in the air, and dissolves readily in hot water. It is a tribasic acid. The sodium salt is sparingly soluble in conc. NaOH; the (Cu-NH_4) salt possesses a characteristic beautiful violet colour. Upon prolonged boiling with hydrochloric acid it is hydrolysed to CO_2 and NH_3, while phosphorus pentachloride converts it into cyanuric chloride.

Only one cyanuric acid is known, and owing to the fact that the N-methyl derivative is obtained by the action of diazo-methane is represented by the iso-structure:

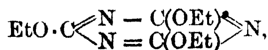


$$O:C\genfrac{}{}{0pt}{}{\diagup NH\cdot CO \diagdown}{\diagdown NH\cdot CO \diagup}NH.$$

(Compare also *Hantzsch*, B. 1906, **39**, 139).

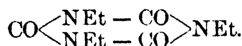
Cyanuric acid is a pseudo acid, as its salts and also chloride have the normal structure. The mercuric salt exists in two isomeric forms.

Two distinct groups of alkyl derivatives are, however, known—**normal cyanuric esters,** *e.g.* **ethyl cyanurate,**



$$EtO\cdot C\genfrac{}{}{0pt}{}{\diagup N - C(OEt) \diagdown}{\diagdown N = C(OEt) \diagup}N,$$

which is formed by the action of ethyl iodide on silver cyanurate at the ordinary temperature, or by the action of sodium ethoxide on cyanogen chloride or cyanuric chloride, is readily cahnged into an **isocyanuric ester**, *e.g.* **ethyl isocyanurate**,



These isocyanurates are often formed instead of the normal compounds if the temperature is not kept low, *e.g.* when a cyanurate is heated with potassium ethyl-sulphate. They are further formed by the polymerization of the isocyanic esters, being thus obtained as by-products in the preparation of the latter.

The constitution of the normal compounds is largely based on the fact that on hydrolysis they behave as normal esters and yield ethyl alcohol and cyanuric acid. The isocyanurates, on the other hand, usually yield primary amines, *e.g.* ethylamine, and hence presumably the alkyl group is attached to nitrogen in the isocyanurate molecule.

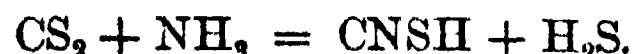
For mixed normal iso-esters, see *Hantzsch* and *Bauer*, B. 1905, 38, 1005.

D. Thiocyanic Acid and its Derivatives

Nearly every oxygen derivative of cyanogen has a sulphur analogue. As examples, we have the salts of thiocyanic acid.

Potassium thiocyanate, *-sulphocyanate, -sulphocyanide, -rhodanide*, CNSK, is readily formed when potassium cyanide is fused with sulphur, or when an aqueous solution of KCN is evaporated with yellow ammonium sulphide.

It is usually prepared by fusing potassium ferrocyanide with sulphur and potashes. It forms long colourless deliquescent prisms, extremely soluble in water with absorption of much heat, and also readily soluble in hot alcohol. **Ammonium thiocyanate**, $CNS(NH_4)$, is formed when a mixture of carbon disulphide, concentrated ammonia, and alcohol (*Millon*) is heated, dithiocarbamate and trithiocarbonate of ammonia being formed as intermediate products:



$$CS_2 + NH_3 = CNSH + H_2S.$$

It forms colourless deliquescent plates, readily soluble in alcohol, and when heated to 130°–140° is partially transformed

into the isomeric thio-urea, just as ammonium cyanate is into urea. It precipitates **silver thiocyanate**, CNSAg (white), from solutions of silver salts, and is therefore employed in the titration of silver, with ferric sulphate as indicator; and it gives with ferric salts a dark blood-red coloration of **ammonium ferrithiocyanate**, $2\,Fe(CNS)_3,\ 9\,NH_4CNS,\ 4\,H_2O$. This last reaction is exceedingly delicate. **Mercurous thiocyanate**, HgCNS, is a white powder insoluble in water, which increases enormously in volume upon being burnt (Pharaoh's serpents). The free **thiocyanic acid**, CNSH, as obtained by decomposing the mercurous salt with hydrochloric acid, is a pale-yellow liquid of pungent odour, but when pure is a colourless solid, m.-pt. 5°. The acid and its salts appear to have the normal structure H·S·C⋮N. At the ordinary temperature it polymerizes to a yellow amorphous substance, and decomposes in concentrated aqueous solution, with formation of **persulphocyanic acid**, $C_2N_2S_3H_2$ (yellow crystals).

Concentrated sulphuric acid decomposes the thiocyanates with formation of carbon oxy-sulphide: $CNSH + H_2O = COS + NH_3$; sulphuretted hydrogen decomposes them into carbon disulphide and ammonia: $CNSH + H_2S = CS_2 + NH_3$.

The alkyl derivatives of thiocyanic acid exist in two distinct forms, corresponding with the normal and iso-cyanates.

Normal Thiocyanates.—Ethyl thiocyanate, $N⋮C·S·CH_2·CH_3$, is obtained either (1) by the distillation of potassium ethyl-sulphate with potassium thiocyanate, or (2) by the action of cyanogen chloride upon ethyl mercaptide. It is a colourless liquid with a peculiar pungent odour of leeks, boils at 142°, and is almost insoluble in water. Alcoholic potash hydrolyses it in the normal manner, yielding ethyl alcohol and potassium thiocyanate; in other reactions, however, the alkyl radical remains united to sulphur; thus nascent hydrogen reduces it to mercaptan, and fuming nitric acid oxidizes it to ethyl-sulphonic acid.

These reactions, combined with its formation from a mercaptide, indicate that the ethyl group is directly attached to sulphur, viz. $C_2H_5·S·C⋮N$.

Allyl thiocyanate, $N⋮C·S·C_3H_5$, is a colourless liquid smelling of leeks. It boils at 161°, and when distilled is converted into the isomeric mustard oil.

The **iso-thiocyanates** are usually known as mustard oils, and are more stable than the normal thiocyanates. They contain the alkyl radical attached to nitrogen, and not to

sulphur (cf. Isocyanates), since on hydrolysis they yield primary amines, *e.g.*:



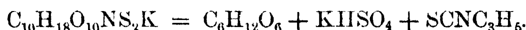
$$S{:}C{:}NEt + 2H_2O = H_2S + CO_2 + NH_2Et,$$

and also on reduction:



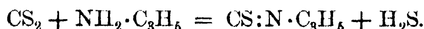
$$S{:}C{:}NEt + 4H = NH_2Et + CH_2S.$$

The thiomethylene formed in this last reaction immediately polymerizes to $(CH_2S)_3$. The commonest iso-thiocyanate is **allyl mustard oil**, commonly known as mustard oil, since the odour and taste of mustard seeds (*Sinapis niger*) are due to this compound. It does not exist as such in the seeds, but is formed from a glucoside, **potassium myronate**, when the seeds are pulverized and left in contact with water. The reaction is a process of fermentation, and is due to the presence of an enzyme, **myrosin**, in the seeds:



$$C_{10}H_{18}O_{10}NS_2K = C_6H_{12}O_6 + KHSO_4 + SCNC_3H_5.$$

It is a liquid sparingly soluble in water and of exceedingly pungent odour, which produces blisters on the skin, and boils at 151°. It is also obtained by distilling allyl thiocyanate, owing to a molecular rearrangement, or by the action of carbon disulphide upon allylamine:



$$CS_2 + NH_2{\cdot}C_3H_5 = CS{:}N{\cdot}C_3H_5 + H_2S.$$

This reaction proceeds in two stages, a dithiocarbamate, $C_3H_5NH{\cdot}CS{\cdot}SNH_3C_3H_5$, the allylamine salt of allyl-dithiocarbamic acid being first formed, and this is changed into allyl iso-thiocyanate when distilled with mercuric chloride. (See Dithiocarbamic acid, p. 306.)

Ethyl iso-thiocyanate, $C_2H_5N{:}CS$ (b.-pt. 134°), and **methyl iso-thiocyanate**, $CH_3N{:}CS$ (solid, m.-pt. 34°, b.-pt. 119°), &c., closely resemble the allyl compound, and are obtained in an analogous manner by the action of carbon disulphide upon ethylamine, methylamine, &c.

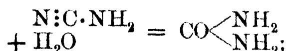
The mustard oils are also obtained by distilling alkylated thio-ureas (p. 307) with syrupy phosphoric acid (*Hofmann*, B. **15**, 985), or with concentrated hydrochloric acid.

E. Cyanamide and its Derivatives

The Amide of Cyanic Acid.—Cyanamide, $N{:}C{\cdot}NH_2$, is formed by leading cyanogen chloride into an ethereal solution

of ammonia, $CNCl + 2NH_3 = CN \cdot NH_2 + NH_4Cl$, or by the action of HgO upon thio-urea in aqueous solution ("desulphurization"), $NH_2 \cdot CS \cdot NH_2 = NC \cdot NH_2 + H_2S$.

It is a colourless crystalline hygroscopic mass, readily soluble in water, alcohol, and ether. It melts at 40°, and when heated to 150° changes into the polymeric dicyan-diamide with explosive ebullition; the same change occurs on evaporating its solution or allowing it to stand. Dilute acids cause it to take up the elements of water, with formation of urea:



$$\begin{matrix} N{:}C \cdot NH_2 \\ + H_2O \end{matrix} = CO\langle\begin{matrix} NH_2 \\ NH_2; \end{matrix}$$

and it combines in an analogous manner with hydrogen sulphide to thio-urea. When heated with ammonium salts, it yields salts of guanidine.

Cyanamide behaves as a weak base, forming crystalline, easily decomposable salts with acids and, at the same time, as a weak acid, yielding a sodium salt, $CN \cdot NHNa$, a lead and a silver salt, &c. The last is a yellow powder, and has the composition CN_2Ag_2.

The calcium derivative of cyanamide, $N{:}C \cdot NCa$, is manufactured for use as a fertilizer, as, in the soil, the nitrogen becomes available for the plant in the form of ammonia. It is manufactured by passing air or nitrogen over calcium carbide at about 800°–1000°,

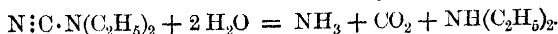


$$CaC_2 + N_2 = CaCN_2 + C,$$

or by passing nitrogen over a mixture of lime and carbon heated to 2000°. An excess of carbon is used, and the crude product, which forms a black powder, contains 14–23 per cent of nitrogen (cf. Abs. 1904, i. 562). The presence of a small amount of calcium chloride accelerates the absorption of nitrogen by calcium carbide.

For constitution, cf. *Werner*, J. C. S. 1915, **107**, 715; also *Colson*, 1917, **111**, 554.

1. **Methyl-** and **ethyl-cyanamides** are prepared for methyl and ethyl thio-urea. **Diethyl-cyanamide**, $CN_2(C_2H_5)_2$, and its homologues are obtained by the action of alkyl iodides or sulphates on crude calcium cyanamide (B. 1911, **44**, 3149). Acids hydrolyse the ethyl compound to CO_2, NH_3, and $NH(C_2H_5)_2$, hence it possesses the structure $N{:}C \cdot N(C_2H_5)_2$:



$$N{:}C \cdot N(C_2H_5)_2 + 2H_2O = NH_3 + CO_2 + NH(C_2H_5)_2.$$

2. Other cyanamide derivatives, which are chiefly known in the aromatic series, are derived from a hypothetical isomer of cyanamide, viz. carbo-di-imide, NH : C : NH; for instance, diphenyl-carbodiimide, $CN_2(C_6H_5)_2$. Boiling with acids likewise decomposes them into CO_2 and an amine, but the latter can only be a primary one.

XIII. CARBONIC ACID DERIVATIVES

Carbonic acid is a dibasic acid, forming two series of salts, *e.g.* Na_2CO_3 and $NaHCO_3$. The acid itself, CO_3H_2, $= O:C{<}^{OH}_{OH}$, is unknown, but may be supposed to exist in the aqueous solution. It is the lowest hydroxy-acid $C_nH_{2n}O_3$, *i.e.* it is homologous with glycollic acid, and may be regarded as hydroxy-formic acid. As both hydroxyls are linked to the same carbon atom, the non-existence of the free hydrate is readily understood (see p. 131, &c.).

The salts of carbonic acid and several simple derivatives of carbon are usually treated of under inorganic chemistry. The esters, chlorides, and amides of carbonic acid, like the salts, form two series. The **normal** compounds, *e.g.* $CO(OC_2H_5)_2$, ethyl carbonate, $COCl_2$, carbonyl chloride, and $CO(NH_2)_2$, carbamide or urea, are well characterized, and are very similar to those of oxalic or succinic acid; the **acid** compounds, *e.g.* $OH \cdot CO \cdot OC_2H_5$, ethyl hydrogen carbonate, $OH \cdot CO \cdot Cl$, chloro-carbonic or chloroformic acid, and $OH \cdot CO \cdot NH_2$, carbamic acid, on the other hand, are unstable in the free state, but form stable salts. Many mixed derivatives are known, *e.g.* ethyl carbamate, $NH_2 \cdot CO \cdot OEt$, which is an ester and an acid amide, analogous to oxamethane (p. 244); $Cl \cdot CO \cdot OC_2H_5$, ethyl chloro-carbonate, which is an ester and an acid chloride.

A. Esters

Ethyl carbonate, $CO(OC_2H_5)_2$, is formed by the action of ethyl iodide upon silver carbonate, or by the action of alcohol upon ethyl chloro-carbonate, and therefore indirectly from carbon oxy-chloride and alcohol:



$$Cl \cdot CO \cdot OC_2H_5 + C_2H_5OH = CO(OC_2H_5)_2 + HCl$$

It is a neutral liquid of agreeable odour, lighter than water, and boils at 126°.

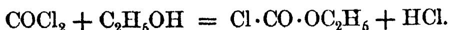
Analogous methyl and **propyl esters** are known, and also esters containing two different alkyl groups. It is a matter of no consequence which of these radicals is introduced first into the molecule, a proof of the symmetrical arrangement of the two hydroxyls.

Ethyl hydrogen carbonate, $HO \cdot CO \cdot O \cdot C_2H_5$, a type of an acid ester, corresponds exactly with ethyl hydrogen sulphate, but is much less stable, and only known in its salts. **Potassium ethyl carbonate**, $KO \cdot CO \cdot OC_2H_5$, is obtained by passing CO_2 into an alcoholic solution of potassic ethoxide: $CO_2 + KOC_2H_5 = CO_3(C_2H_5)K$. It crystallizes in glistening mother-of-pearl plates, but is decomposed by water into potassium carbonate and alcohol.

B. Chlorides of Carbonic Acid

Carbon oxy-chloride, *Carbonyl chloride*, *phosgene*, $COCl_2$ (*J. Davy*), is the true chloride of carbonic acid and is analogous to sulphuryl chloride, SO_2Cl_2. It is obtained by the direct combination of carbon monoxide and chlorine in sunlight, and also by the oxidation of chloroform by means of chromic acid. It is a colourless gas, condensing to a liquid below +8°, of exceptionally suffocating odour, and is readily soluble in benzene or toluene. As an acid chloride it decomposes violently with water into CO_2 and HCl. It therefore transforms hydrated acids into their anhydrides, with separation of water, and converts aldehyde into ethylidene chloride. It yields urea derivatives with secondary amines of the fatty series, and carbamic chlorides with secondary amines of the aromatic (B. **20**, 783).

Chloro-carbonic acid, *Chloro-formic acid*, $Cl \cdot CO \cdot OH$, the half acid chloride of carbonic acid, is analogous to chloroxalic acid (p. 242), but is so unstable that it is unknown in the free state. Its **esters**, however, *e.g.* **ethyl chloro-carbonate, ethyl chloro-formate**, $Cl \cdot CO \cdot OC_2H_5$, may be prepared by the action of carbon oxy-chloride upon alcohols (*Dumas*, 1833):



$$COCl_2 + C_2H_5OH = Cl \cdot CO \cdot OC_2H_5 + HCl.$$

The ethyl ester is a volatile liquid of very pungent odour, which boils at 93°. It reacts as an acid chloride, being decom-

posed by water, and is specially fitted to effect the synthetical entrance of the carboxyl group into many compounds.

The esters and acid chlorides just described are derived from ordinary carbonic acid, H_2CO_3, the analogue of meta-silicic acid, H_2SiO_3. Although an ortho-carbonic acid itself, $C(OH)_4$, is unknown, certain derivatives are readily prepared. **Carbon tetrachloride** may be regarded as the chloride of ortho-carbonic acid. It is much more stable than ordinary acid chlorides, and at high temperatures only is it decomposed by alkalis, yielding alkali chloride and carbonate.

The esters of ortho-carbonic acid, *e.g.* **ethyl ortho-carbonate**, $C(OC_2H_5)_4$, are readily obtained by the action of sodium alcoholates on chloropicrin (p. 100). They are colourless oils with fragrant odours. The **ethyl** ester boils at 158°, and the **propyl** at 224°. When hydrolysed, they yield an alkali carbonate and the alcohol.

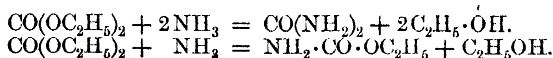
C. Amides of Carbonic Acid

The normal amide of carbonic acid is **urea** or **carbamide**, $NH_2\cdot CO\cdot NH_2$, the amic acid is **carbamic acid**, $HO\cdot CO\cdot NH_2$. **Imido-carbonic acid**, $HN{:}C(OH)_2$, would be an imide of carbonic acid, but it is only known in its derivatives (*Sandmeyer*, B. **19**, 862).

The amidine of carbonic acid is **guanidine**. The "ortho-amide" of carbonic acid, which would possess the formula $C(NH_2)_4$, is unknown; when it might be expected, guanidine and ammonia are formed instead.

The modes of *formation* of urea and of carbamic acid are exactly analogous to those of the amides in general:

1. By the action of ammonia upon ethyl carbonate:



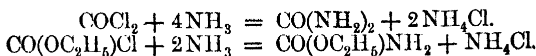
$$CO(OC_2H_5)_2 + 2NH_3 = CO(NH_2)_2 + 2C_2H_5\cdot OH.$$
$$CO(OC_2H_5)_2 + NH_3 = NH_2\cdot CO\cdot OC_2H_5 + C_2H_5OH.$$

2. By the abstraction of the elements of water from carbonate or carbamate of ammonia. Dry carbon dioxide and ammonia combine together directly to ammonium carbamate the so-called anhydrous carbonate of ammonia, $NH_2\cdot CO\cdot ONH_4$, which is transformed into urea when heated to 135°, or when exposed to the action of an alternating current of electricity:



$$NH_2\cdot CO\cdot ONH_4 = CO(NH_2)_2 + H_2O.$$

3. By the action of ammonia upon carbonyl chloride and its derivatives:



$$COCl_2 + 4NH_3 = CO(NH_2)_2 + 2NH_4Cl.$$
$$CO(OC_2H_5)Cl + 2NH_3 = CO(OC_2H_5)NH_2 + NH_4Cl.$$

Carbamic acid, $NH_2 \cdot CO \cdot OH$, is known only in the form of derivatives; the *ammonium* salt, $NH_2 \cdot CO \cdot ONH_4$, forms a white mass, and dissociates at 60° into $2NH_3 + CO_2$. Its aqueous solution does not precipitate a solution of calcium chloride at the ordinary temperature; but when boiled it is hydrolysed to the carbonate, and calcium carbonate is then thrown down.

Urethane, *Ethyl carbamate*, $NH_2 \cdot CO \cdot OC_2H_5$, is formed according to method 3, and by the direct union of cyanic acid with alcohol; also from urea nitrate and sodium nitrite in presence of alcohol. It forms large plates, is readily soluble in water, melts at 50°, and boils at 184°. It acts as a soporific, and on hydrolysis with alkali yields the alkali carbonate, ammonia and ethyl alcohol. One of its hydrogen atoms is replaceable by sodium. Urethane may be employed instead of cyanic acid for certain synthetic reactions (B. **23**, 1856).

Analogous **methyl** and **propyl esters** of carbamic acid are known, and are also termed urethanes.

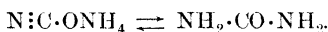
Carbamic chloride, $NH_2 \cdot CO \cdot Cl$, obtained by the action of hydrogen chloride upon cyanic acid (*Wohler*, A. **45**, 357), and of carbonyl chloride upon ammonium chloride at 400°, forms long, compact, colourless needles of pungent odour. M.-pt. 50°, b.-pt. 61°–62°. It reacts violently with water, amines, &c., and serves for the synthesis of organic acids (see these).

Ethyl imido-dicarboxylate, $NH(CO_2C_2H_5)_2$, is the imide corresponding with the amide urethane. It may be prepared from the sodium compound of urethane and ethyl chlorocarbonate. It forms colourless crystals, melting at 50°. By the exchange of one ethoxy (OC_2H_5) group for an amido (NH_2) group, it gives rise to allophanic ester, and by the exchange of two, to biuret (see p. 300).

Urea, *Carbamide*, $CO(NH_2)_2$, was first found in urine in 1773. It is contained in the urine of mammals, birds, and some reptiles, and also in other animal fluids. An adult man produces about 30 gms. daily, and it may be regarded as the final decomposition product formed by the oxidation of the nitrogenous compounds in the organism.

It has been shown that ammonium cyanate and urea are formed when a very dilute solution of glucose (p. 320) in strong ammonia is oxidised. Larger yields are obtained by oxidising an ammoniacal solution of formaldehyde. It is possible that this represents the changes which take place in the animal system, viz. glucose → formaldehyde → ammonium cyanate → carbamide (*Fosse*, C. R. 1919, **168**, 164).

It may be prepared by the action of ammonia on ethyl carbonate, ethyl carbamate, or phosgene, and synthetically by the molecular transformation of ammonium cyanate, by warming its aqueous solution or allowing it to stand (cf. pp. 1 and 282):



$$N{:}C{\cdot}ONH_4 \rightleftharpoons NH_2{\cdot}CO{\cdot}NH_2.$$

The reaction is reversible, and hence the process is never complete. When equilibrium is reached, only a very small amount of untransformed cyanate is left, and the equilibrium is practically independent of the temperature. The reaction has been shown to be a typical bimolecular one (*Walker* and *Hambly*, J. C. S. 1895, 746).

The reaction is represented as follows by *Chattaway* (J. C. S. 1912, **101**, 170. Compare also *Werner*, *ibid.* 1913, **103**, 1010, 2275; 1914, **105**, 926):



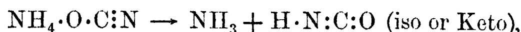
$$NH_4{\cdot}N{:}C{:}O \rightarrow HN{:}C{:}O + NH_3 \rightarrow HN{:}C(OH)NH_2 \rightarrow NH_2{\cdot}CO{\cdot}NH_2.$$

According to *Chattaway* the isocarbamide, $HN{:}C\langle{}^{OH}_{NH_2}$, is first formed, and then passes over into the true amide. *Werner*, on the other hand, concludes that ammonium cyanate has the normal structure $H_4N{\cdot}O{\cdot}C{:}N$. At low temperatures this exists in the state of equilibrium:



$$NH_4{\cdot}O{\cdot}C{:}N \rightleftharpoons NH_3 + OH{\cdot}C{:}N \text{ (normal or Enol)},$$

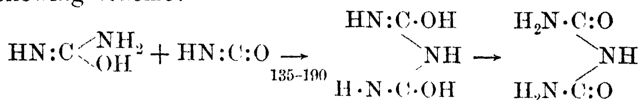
but at higher temperatures:



$$NH_4{\cdot}O{\cdot}C{:}N \rightarrow NH_3 + H{\cdot}N{:}C{:}O \text{ (iso or Keto)},$$

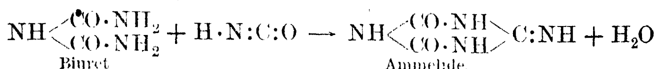
and that the ammonia and iso-form can react to produce urea, to which the cyclic structure $H{\cdot}N{:}C\langle{}^{NH_3}_{O}$ is attributed. This formula is in perfect harmony with the fact that when urea is heated it breaks up into ammonia and cyanic acid, the latter of which polymerizes to cyanuric acid, biuret, and

ammelide. The formation of biuret is represented by the following scheme:



$$HN{:}C\begin{matrix}\diagup NH_2\\ \diagdown OH\end{matrix} + HN{:}C{:}O \xrightarrow[135-190]{} \begin{matrix}HN{:}C{\cdot}OH\\ \diagdown NH\\ H{\cdot}N{\cdot}C{\cdot}OH\end{matrix} \rightarrow \begin{matrix}H_2N{\cdot}C{:}O\\ \diagdown NH\\ H_2N{\cdot}C{:}O\end{matrix}$$

and of ammelide, as:

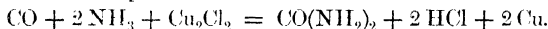


$$\underset{\text{Biuret}}{NH\begin{matrix}\diagup CO{\cdot}NH_2\\ \diagdown CO{\cdot}NH_2\end{matrix}} + H{\cdot}N{:}C{:}O \rightarrow \underset{\text{Ammelide.}}{NH\begin{matrix}\diagup CO{\cdot}NH\diagdown\\ \diagdown CO{\cdot}NH\diagup\end{matrix}C{:}NH} + H_2O$$

It is interesting to note that when urea and its homologues are methylated by means of methyl sulphate O-methyl derivatives, *e.g.* $HN{:}C(NH_2)OMe$, are formed (*Werner*).

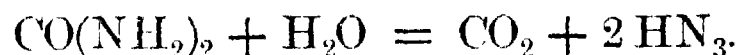
It is usually prepared by mixing a solution of potassium cyanate (from the ferrocyanide) with ammonium sulphate and evaporating the mixture (ammonium cyanate is first formed and gradually changes to urea), or by evaporating urine, adding nitric acid, and decomposing the separated and purified nitrate of urea by barium carbonate.

It is also formed by heating a solution of carbon monoxide in ammoniacal cuprous chloride:



$$CO + 2\,NH_3 + Cu_2Cl_2 = CO(NH_2)_2 + 2\,HCl + 2\,Cu.$$

It crystallizes in long rhombic prisms or needles, has a cooling taste, is very readily soluble in water, also in alcohol, but not in ether. It melts at 132°, sublimes *in vacuo* without decomposition, and when strongly heated yields ammonia, cyanuric acid, biuret, and ammelide. As an amide it is readily hydrolysed by boiling with alkalis or acids, or by superheating with water (cf. *Fawsitt*, J. C. S. 1904, 1581; 1905, 494):



$$CO(NH_2)_2 + H_2O = CO_2 + 2\,HN_3.$$

It forms a definite compound with hydrogen peroxide.

Nitrous acid reacts with it to produce carbon dioxide, nitrogen, and water:



$$CO(NH_2)_2 + 2\,NO_2H = CO_2 + 2\,N_2 + 3\,H_2O.$$

Sodium hypochlorite and hypobromite act in a similar manner (*Davy*, *Knop*). *Hüfner's* method of estimating urea quantitatively depends upon the measurement of the nitrogen thus obtained (J. pr. Ch., [2], **3**, 1; cf. also B. **24**, Ref. 330). Urea also reacts with bromine and alkalis in much the same manner as the lower acid amides (*Hofmann* reaction p. 191), yielding carbon dioxide and the corresponding amine, hydra-

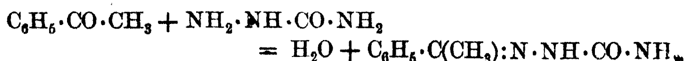
zine (C. Z. 1905, i, 1227), which is best removed by the addition of benzaldehyde. Urea is readily estimated by conversion into ammonia, either by heating with pure crystallized magnesium chloride and a little hydrochloric acid or by means of an enzyme (a urease) contained in soya beans.

Urea reacts with an aqueous solution of chlorine, yielding the dichloro-derivative $CO(NHCl)_2$. With acids this forms nitrogen trichloride, and with ammonia it yields diurea or paraurazine, $CO<\begin{smallmatrix}NH\cdot NH\\NH\cdot NH\end{smallmatrix}>CO$ (*Chattaway*, J. C. S. 1909, 129, 235). When warmed with alcoholic potash to 100°, urea is converted into cyanate of potassium and ammonia.

The basic character of the amino groups is greatly weakened in urea by the presence of the negative carbonyl. Among the salts of urea with acids may be mentioned **urea nitrate**, CON_2H_4, HNO_3, which crystallizes in glistening white plates, readily soluble in water, but only slightly in nitric acid; also the **chloride, oxalate,** and **phosphate**. But like acetamide, urea also forms salts with metallic oxides, especially with mercuric oxide, *e.g.* CON_2H_4, $2HgO$; finally, it yields crystalline compounds with salts, *e.g.* urea **sodium chloride**, CON_2H_4, $NaCl$, H_2O (glistening prisms), and **urea silver nitrate**, CON_2H_4, $AgNO_3$ (rhombic prisms). The precipitate which is obtained on adding mercuric nitrate to a neutral aqueous solution of urea has the formula $2CON_2H_4$, $Hg(NO_3)_2$, $3HgO$; upon its formation depends *Liebig's* method for titrating urea. (See the memoirs of *Pflüger* and *Bohland* on the subject, *e.g.* *Pflüger*, Arch. f. Phys. 38, 575.)

Isomeric with urea is the amidoxime, **isuret** or methane amidoxime, $NH:CH\cdot NH\cdot OH$, which is obtained from HCN and NH_2OH; it crystallizes in prisms (see p. 188).

Closely related to carbamide, $NH_2\cdot CO\cdot NH_2$, is **semicarbazide** or semihydrocarbazide, $NH_2\cdot CO\cdot NH\cdot NH_2$, which is the half amide and half hydrazide of carbonic acid. It may be prepared from potassium cyanate and hydrazine hydrate. It is a basic substance, melts at 96°, and is usually met with in the form of its hydrochloride. It reacts with aldehydes and ketones in much the same manner as phenyl-hydrazine, yielding condensation products known as **semicarbazones**:

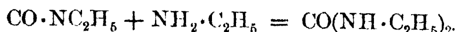


$$C_6H_5\cdot CO\cdot CH_3 + NH_2\cdot NH\cdot CO\cdot NH_2$$
$$= H_2O + C_6H_5\cdot C(CH_3):N\cdot NH\cdot CO\cdot NH_2.$$

which crystallize well, and have well-defined melting-points (see p. 143).

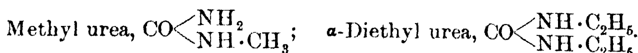
Alkylated ureas are obtained by the exchange of the amido-hydrogen atoms for one or more alkyl radicals.

They are produced by *Wohler's* synthetical method, viz. by the combination of cyanic acid with amines, or of cyanic esters with ammonia or amines, thus:—

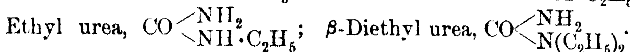


$$CO\cdot NC_2H_5 + NH_2\cdot C_2H_5 = CO(NH\cdot C_2H_5)_2.$$

Also from amines and carbon oxy-chloride. As examples may be mentioned:



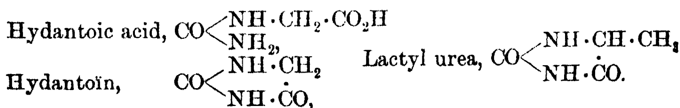
Methyl urea, $CO<^{NH_2}_{NH\cdot CH_3}$; α-Diethyl urea, $CO<^{NH\cdot C_2H_5}_{NH\cdot C_2H_5}$.



Ethyl urea, $CO<^{NH_2}_{NH\cdot C_2H_5}$; β-Diethyl urea, $CO<^{NH_2}_{N(C_2H_5)_2}$.

Certain of them closely resemble urea; others, however, are liquid and volatilize without decomposition. Their *constitution* follows very simply from the nature of the products which are formed on hydrolysis; thus α-diethyl urea breaks up into carbon dioxide and ethylamine, and the β-compound into carbon dioxide, ammonia, and diethylamine, in accordance with the generalization enunciated on p. 98, that alkyl radicals which are directly united to nitrogen are not separated from it on hydrolysis.

Acyl Derivatives.—By the entrance of acyl radicals into urea, its acid derivatives or **ureides** are formed. These are formed by the action of acid chlorides or anhydrides upon urea, or by the action of phosphorus oxy-chloride upon the salts of urea with organic acids. The simple ureides correspond in many respects with acid amides or anilides, have neither distinctly acid nor basic properties, and may be hydrolysed to the acid and urea or its products of decomposition (p. 293). To this class belong **acetyl urea,** $NH_2\cdot CO\cdot NH\cdot CO\cdot CH_3$, and **allophanic acid,** $NH_2\cdot CO\cdot NH\cdot CO_2H$. Hydroxy-monobasic acids also form ureides, not only in virtue of their acidic nature, but as alcohol and acid at the same time, thus:—



Hydantoic acid, $CO<^{NH\cdot CH_2\cdot CO_2H}_{NH_2}$,

Hydantoïn, $CO<^{NH\cdot CH_2}_{NH\cdot CO}$,

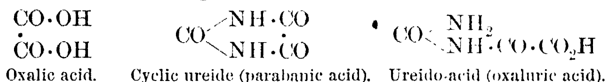
Lactyl urea, $CO<^{NH\cdot CH\cdot CH_3}_{NH\cdot CO}$.

Hydantoïn or *glycolyl urea* (needles, neutral) and **hydantoic**

acid or *glycoluric acid* (prisms), are derivatives of glycollic acid; the former on hydrolysis yields hydantoic acid, which in its turn is broken up into CO_2, NH_3, and glycocoll. They are obtained from certain uric acid derivatives (*e.g.* allantoïn) by the action of hydriodic acid, and also synthetically, for instance, hydantoic acid from glycocoll and cyanic acid. A **methyl-hydantoïn**, $C_3H_3(CH_3)N_2O_2$, results from the partial hydrolysis of creatinine (p. 308), NH being replaced by O.

Substituted hydantoins are also formed by the action of hypochlorites or hypobromites on dialkylated malonamides, *e.g.* diethylmalonamide, $CEt_2(CONH_2)_2$, gives diethylhydantoin.

Just as the dibasic acids—oxalic, malonic, tartronic, and mesoxalic—yield amides with ammonia, so with urea they form compounds of an amidic nature. In such reactions either two molecules of water are eliminated, so that no carboxyl remains in the compound, or only one molecule is eliminated and a carboxyl group is retained. In the former case the so-called **cyclic ureides** are obtained, and in the latter the **ureido-acids**, *e.g.* from oxalic acid, parabanic and oxaluric acids:

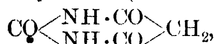


Oxalic acid. Cyclic ureide (parabanic acid). Ureido-acid (oxaluric acid).

In an analogous manner the ureide barbituric acid, $C_4H_4N_2O_3$, is derived from malonic acid, the ureide dialuric acid, $C_4H_4N_2O_4$, from tartronic acid, and the ureide alloxan, $C_4H_2N_2O_4$, and ureido-acid alloxanic acid, $C_4H_4N_2O_5$, from mesoxalic acid. These are solid and, for the most part, beautifully crystallizing compounds of a normal amidic character, and therefore readily hydrolysed to urea (or CO_2 and NH_3) and the respective acid. The ureido-acids may be regarded as half-hydrolysed ureides, and may be prepared from the latter in this manner. As they contain a carboxyl group, they still possess acidic properties.

The constitution of the various cyclic ureides and ureido-acids follows in most cases from the products they yield on hydrolysis, and also from their synthetical methods of formation and their relationships to one another.

Some of these ureides are obtained synthetically from urea and the requisite acid often in the presence of phosphorus oxy-chloride, *e.g.* malonyl-urea (barbituric acid),



from urea and malonic acid. Many can be obtained by the

oxidation of various complex natural products, *e.g.* alloxan or parabanic acid by oxidizing uric acid with nitric acid.

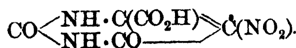
Most of the ureides have the character of more or less strong acids. Since this acid character is not to be explained, as in the case of the ureido-acids, by the presence of carboxyl groups, one must assume that it depends upon reasons similar to those which apply in the case of cyanic acid and of succinimide, viz. that the replaceable hydrogen atoms are imido-hydrogen atoms, the acidic nature of which is determined by the adjacent carbonyl groups. This explains, for instance, why parabanic acid is a strong dibasic acid.

Only a few of the more important among these compounds can be discussed here. The names given to the majority of them have no relationship to their constitution, and were assigned to them before the constitutions had been determined.

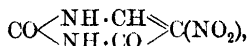
Parabanic acid, *Oxalyl urea,* $CO\langle^{NH \cdot CO}_{NH \cdot CO}$ is prepared by the action of nitric acid upon uric acid, or of oxalyl chloride on urea, and crystallizes in needles or prisms soluble in water and alcohol. The salts, *e.g.* $C_3HKN_2O_3$, $C_3Ag_2N_2O_3$, are unstable, being converted by water into salts of **oxaluric acid,** $NH_2 \cdot CO \cdot NH \cdot CO \cdot CO_2H$, which crystallize well.

A **methyl-parabanic** acid, $CO\langle^{NMe \cdot CO}_{NH—CO}$, and a **dimethyl-parabanic** acid, the so-called **"cholestrophane",** $CO\langle^{NMe \cdot CO}_{NMe \cdot CO}$, are also known. The former is prepared by the action of nitric acid upon methyl-uric acid, and crystallizes in prisms, while the latter is obtained from theine with nitric acid or chlorine water, and also by the methylation of parabanic acid, *i.e.* from the silver salt and methyl iodide. It crystallizes in plates and distils without decomposition.

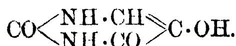
Methyl-uracyl, $CO\langle^{NH \cdot C(CH_3)}_{NH \cdot CO —}\rangle CH$, is produced by the action of urea upon acetoacetic ester, water and alcohol being eliminated (*Behrend,* A. **229**, 1, and p. 238). When it is treated with nitric acid, a nitro-group enters the molecule, and the methyl-group is oxidized to carboxyl, thus forming **5-nitro-uracyl-4-carboxylic acid,**


$$CO\langle^{NH \cdot C(CO_2H)}_{NH \cdot CO —}\rangle C(NO_2).$$

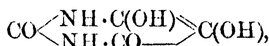
This in its turn can give up carbon dioxide and pass into **5-nitro-uracyl**,



which yields upon reduction with tin and hydrochloric acid 5-amino-uracyl and **isobarbituric acid**, *5-hydroxy-uracyl*,



This last is oxidized by bromine water to **isodialuric acid**,



from which uric acid may be synthesised by warming with urea and sulphuric acid (see p. 301).

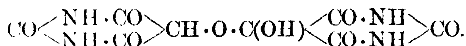
Barbituric acid, *Malonyl urea*, $CO{<}^{NH\cdot CO}_{NH\cdot CO}{>}CH_2$, crystallizes in large colourless prisms ($+ 2\,H_2O$). The hydrogen atoms of the methylene group are reactive (cf. ethyl malonate), and can be replaced by bromine, $\cdot NO_2$, $:N\cdot OH$, metals, &c. The metallic radicals* in their turn can be replaced by alkyl groups. The dimethyl derivative when hydrolysed yields carbon dioxide, ammonia, and dimethylmalonic acid, thus indicating that the methyl groups have replaced the methylene hydrogen atoms. The *iso*-nitroso derivative, $CO{<}^{NH\cdot CO}_{NH\cdot CO}{>}C:N\cdot OH$, **violuric acid**, can also be obtained by the action of hydroxylamine on alloxan, and on reduction yields **amino-barbituric acid** (uramil), from which pseudouric and uric acids have been synthesised (p. 301). **Diethylbarbituric acid** (*veronal*) is used as a soporific.

Dialuric acid, *Tartronyl urea*, $CO{<}^{NH\cdot CO}_{NH\cdot CO}{>}CH\cdot OH$, crystallizes in colourless needles or prisms which redden in the air. It is a strong dibasic acid, and on oxidation yields alloxantin.

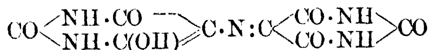
Alloxan, *Mesoxalyl urea*, $CO{<}^{NH\cdot CO}_{NH\cdot CO}{>}CO$, may be prepared from uric acid by oxidation with cold HNO_3. It forms large colourless glistening rhombic prisms ($+4\,H_2O$), is readily soluble in water, and has strongly acidic properties. It colours the skin purple-red, and with ferrous sulphate solution produces an indigo-blue colour. It combines with $NaHSO_3$, and

readily changes into alloxantin. The corresponding ureido-acid, **alloxanic acid**, $NH_2 \cdot CO \cdot NH \cdot CO \cdot CO \cdot CO_2H$, which alloxan yields even with cold alkali, forms a radiating crystalline mass readily soluble in water. **Methyl- and dimethyl alloxan** are also known, and may be obtained by the action of nitric acid upon methyl-uric acid and caffeine respectively.

The diureide **alloxantin**, $C_8H_4O_7N_4$, stands midway in composition between tartronyl- and mesoxalyl-urea, by the combination of which it is formed. It may also be obtained by the action of H_2S on alloxan, or directly from uric acid and HNO_3. It crystallizes in small hard prisms ($+ 3H_2O$), which become red in air containing ammonia, their solution acquiring a deep-blue colour on the addition of ferric chloride and ammonia. The tetramethyl derivative, **amalic acid**, $C_8(CH_3)_4N_4O_7$, is obtained by oxidizing theine with chlorine water, and forms colourless crystals which redden the skin and whose solution is turned violet-blue by alkali. Both these compounds yield, upon oxidation, first alloxan or its dimethyl derivative, and then parabanic or dimethyl-parabanic acid. Alloxantin probably has the constitution:

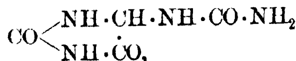


When heated with ammonia it is converted into **murexide**, the acid ammonium salt of **purpuric acid**, $C_8H_5N_6O_5$, which is the acid form of barbituryl iminoalloxan:



(J. pr. 1905, [ii], **73**, 449), which is formed when uric acid is evaporated with dilute nitric acid, and ammonia added to the residue; this constitutes the "**murexide test**" for uric acid. Murexide crystallizes in four-sided plates or prisms ($+ H_2O$) of a golden-green colour, which dissolve to a purple-red solution in water and to a blue one in potash. The free acid is incapable of existence.

Allantoïn is a diureide of glyoxylic acid, of the constitution



and is found in the allantoic liquid of the cow, the urine of

sucking calves, &c. It forms glistening prisms, and can be synthesized from its components.

Biuret, $NH_2 \cdot CO \cdot NH \cdot CO \cdot NH_2$, is obtained by heating urea at 160° (for mechanism, cf. *Werner*, J. C. S. 1913, **103**, 2278).



$$2NH_2 \cdot CO \cdot NH_2 = NH_3 + NH(CO \cdot NH_2)_2.$$

It crystallizes in white needles ($+ H_2O$), and is readily soluble in water and alcohol. The alkaline solution gives a beautiful violet-red coloration on the addition of a little cupric sulphate—the "**biuret reaction**". Biuret is also formed by the action of ammonia upon the **allophanic esters**, crystalline compounds sparingly soluble in water, which are prepared from urea and chloro-carbonic esters, thus:—



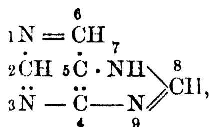
$$CO(NH_2)_2 + Cl \cdot CO_2C_2H_5 = NH_2 \cdot CO \cdot NH \cdot CO_2C_2H_5 + HCl.$$

Allophanic acid itself is not known in the free state, as it immediately breaks up into urea and carbon dioxide. Biuret may be regarded as its amide.

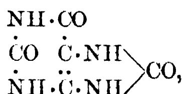
The Purine Group (*E. Fischer*, B. 1899, **32**, 435; **35**, 2564).—A number of relatively complex cyclic diureides derived from 1 molecule of hydroxy dibasic acids and 2 of urea are known. One of the most important of these is **uric acid**.

The parent substance of this group of compounds is **purine** (*E. Fischer*, B. 1899, **32**, 449).

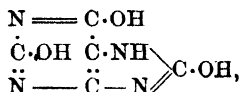
Purine:



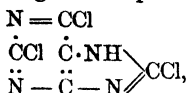
is usually obtained from uric acid:



which reacts with phosphorus oxy-chloride as the tautomeric trihydroxy purine:

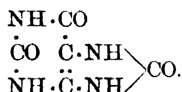


yielding the corresponding trichlorpurine:



and this on reduction yields purine itself. It is a colourless crystalline compound, melts at 216°, and is both an acid and a base. It dissolves readily in water, and is not easily oxidized. The atoms of the ring are usually numbered as indicated.

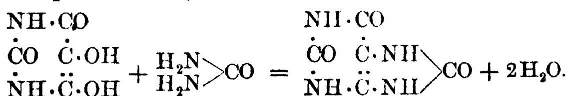
Uric acid is the keto form of 2:6:8-*trihydroxy-purine*, and has the constitutional formula:



Uric acid and many other compounds containing the ·NH·CO· group, as tautomeric substances, behave in certain reactions as ketonic compounds and in other reactions as hydroxylic derivatives, *i.e.* they exhibit keto-enolic tautomerism. It is a common constituent of the urine of most carnivorous animals, whereas that of herbivorous animals contains hippuric acid. It is also found in the blood and muscle juices of the same animals, and would appear to be the oxidation product of the complex nitrogenous compounds contained in the organism. It is also contained in the excrement of birds, serpents, and insects, and in guano.

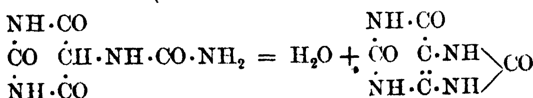
Syntheses.—1. By heating glycocoll with urea (*Horbaczewski*, B. **15**, 2678).

2. By heating isodialuric acid (p. 298) with urea and concentrated sulphuric acid (*R. Behrend* and *O. Roosen*, A. **251**, 235):

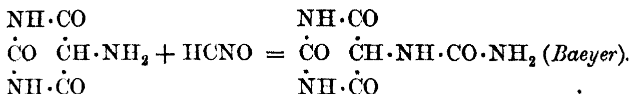


3. By heating cyano-acetic acid with urea (*Traube*, B. 1891, **24**, 3419; 1900, **33**, 3035).

4. By heating pseudouric acid with hydrochloric acid when water is eliminated (*E. Fischer*, B. 1897, **30**, 559):



The pseudo acid is obtained as the potassium salt by the condensation of amino-barbituric acid (p. 298) with potassic cyanate:


NH·CO NH·CO
CO CH·NH₂ + HCNO = CO CH·NH·CO·NH₂ (*Baeyer*).
NH·CO NH·CO

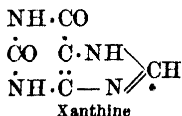
It is usually prepared from guano and the excrement of serpents, and crystallizes in small plates; is almost insoluble in water, and quite insoluble in alcohol or ether. Uric acid is a weak dibasic acid; its common salts are the acid ones, *e.g.* $C_5H_3O_3N_4K$, a powder sparingly soluble in water. The lithium and piperazine salts are somewhat more soluble, and hence are used in medicine for removing uric acid from the human system.

When the two lead salts are treated with methyl iodide, **methyl- and dimethyl uric acids** are obtained, both of which also are weak dibasic acids, since they still contain replaceable imido-hydrogen atoms.

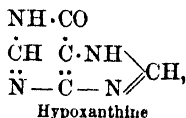
Constitution.—The constitutional formula, given above, was first proposed by *Medicus*, and afterwards proved to be correct by *E. Fischer* (A. **215**, 253). The more important arguments used were:—(1) Uric acid yields alloxan and urea when cautiously oxidized, this proving that we have to deal here with a carbonic acid derivative and a carbon chain, C·C·C; (2) uric acid contains four imido groups, since, by the introduction of four methyl groups, one after the other, four monomethyl, various di- and trimethyl, and one tetramethyl uric acids are obtained. When the tetramethyl acid is hydrolysed with concentrated hydrochloric acid all the nitrogen is eliminated as methylamine, and thus each methyl group is probably attached to a nitrogen atom; (3) dimethyluric acid yields methylalloxan and methylurea on oxidation.

Uric acid is usually recognized by its sparing solubility, and by its giving the murexide test.

Xanthine, 2:6-*Dihydroxy-purine*, or the corresponding keto form:



Xanthine

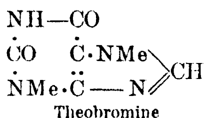


Hypoxanthine

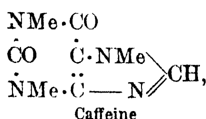
may be obtained by the reduction of uric acid with sodium amalgam, or by the action of nitrous acid on guanine (amino hypoxanthine). It is a white amorphous mass, and is both basic and acidic. The lead salt, $C_5H_2PbN_4O_2$, is converted into theobromine by methyl iodide. (Cf. B. 1897, **30**, 2235; 1900, **33**, 3035.) When oxidized it yields the same products as uric acid.

Hypoxanthine, *Sarcine*, or 6-*oxy-purine*, is sparingly soluble in water and closely resembles xanthine.

Theobromine, 3:7-*Dimethyl-xanthine*,



Theobromine



Caffeine

occurs in the beans of cacao; it is a crystalline powder of bitter taste, and is only sparingly soluble in water and alcohol. It forms salts both as a base and as an acid. The silver salt, $C_7H_7AgN_4O_2$, when treated with CH_3I, yields **caffeine** or **theine**, 1:3:7-*trimethyl-xanthine*, which occurs in tea (2–4 per cent), coffee, and various plants. (For synthesis from dimethyl urea and malonic acid, see *Fischer*, B. 1895, **28**, 3137; 1899, **32**, 435; from cyanoacetic acid, 1900, **33**, 3035.) It crystallizes (+ H_2O) in beautiful long glistening silky needles of faintly bitter taste, which are sparingly soluble in cold water and alcohol, and can be sublimed. The salts are readily decomposed by water. Chlorine oxidizes it to dimethyl alloxan and monomethyl urea. **Theophylline,** 1:3-*dimethyl-xanthine*, also occurs in tea.

Guanine, 2-*amino*-6-*oxy-purine*, or 2-*amino-hypoxanthine*, and **adenine,** 6-*amino-purine*, both contain amino-groups, and are thus basic substances. Both compounds, together with xanthine and hypoxanthine, are formed by the decomposition of the nucleic acids and other complex compounds contained in the animal system. The constitution follows largely from (1) basic properties, (2) their conversion respectively into xanthine and hypoxanthine by the aid of nitrous acid, and (3) from their oxidation products.

A summary of some of the more important ureides which can be obtained from uric acid are tabulated on p. 304.

For other uric acid derivatives, cf. *Biltz*, A. 1916, **413**, 1–206; 1917, **414**, 54.

PRODUCTS OBTAINABLE FROM URIC ACID

1. On Oxidation.			2. On Reduction.	3. With PCl_5.
(*a*)	(*b*)	(*c*)		
With dilute HNO_3, ↓ Alloxan, $CO<\genfrac{}{}{0pt}{}{NH\cdot CO}{NH\cdot CO}>CO$, ↓ reduced. Dialuric acid, $CO<\genfrac{}{}{0pt}{}{NH\cdot CO}{NH\cdot CO}>CH\cdot OH$, ↓ reduced. Barbituric acid, $CO<\genfrac{}{}{0pt}{}{NH\cdot CO}{NH\cdot CO}>CH_2$, Alloxan and dialuric acid give alloxantin, $CO<\genfrac{}{}{0pt}{}{NH\cdot CO}{NH\cdot CO}>C\cdot C<\genfrac{}{}{0pt}{}{CO\cdot NH}{CO\cdot NH}>CO$. (the two C atoms bridged by O)	With concentrated HNO_3. ↓ Parabanic acid, $CO<\genfrac{}{}{0pt}{}{NH\cdot CO}{NH\cdot CO}$, ↓ with KOH. Oxaluric acid, $CO<\genfrac{}{}{0pt}{}{NH\cdot CO\cdot COOH}{NH_2}$.	In alkaline solution. ↓ Allantoïn. $CO<\genfrac{}{}{0pt}{}{NH\cdot CH\cdot NH\cdot CO\cdot NH_2}{NH\cdot CO}$, ↓ reduced. Hydantoïn, $CO<\genfrac{}{}{0pt}{}{NH\cdot CH_2}{NH\cdot CO}$. ↓ Hydrolysed Allantoic acid, $CO<\genfrac{}{}{0pt}{}{NH\cdot CH_2\cdot NH\cdot CO\cdot NH_2}{NH\cdot CO_2H}$.	Electrolytically. ↓ $NH\cdot CH_2$ $CO\quad CH\cdot NH$ $NH\cdot CH\cdot NH$ $>CO$, Purone. With sodium amalgam ↓ Xanthine, $NH\cdot CO$ $CO\quad C\cdot NH$ $NH\cdot C—N$ $>CH$.	Trichloro-purine, ↓ reduced. Purine, $N=CH$ $CH\quad C\cdot NH$ $N—C—N$ $>CH$. Xanthine, hypoxanthine, guanine, and adenine can also be obtained from trichloro-purine (B. 1897, **30**, 2220, 2226).

For details of oxidation with hydrogen peroxide, cf. *Venable* and others, J. A. C. S. 1917, **39**, 1750; 1918, **40**, 1099, 1120.

D. Sulphur Derivatives of Carbonic Acid

In addition to most of the carbonic acid derivatives which have been described, there exist analogous compounds in which the oxygen is wholly or partially replaced by sulphur. Many of these again are unstable in the free state, from the fact of their being too readily hydrolysed to CO_2, COS, or CS_2, but they are known as salts, or at least as esters. The latter are often not real esters, in so far that those which contain an alkyl radical linked to sulphur do not yield the corresponding alcohols on hydrolysis, but mercaptans, in accordance with the intimate character of this linking.

Various mono-, di-, and tri-thio-derivatives of carbonic acid are known, according as 1, 2, or 3 of the oxygen atoms are replaced by sulphur.

Many of the thio-acids react as tautomeric substances, and give rise to isomeric alkyl derivatives in exactly the same manner as hydrocyanic, cyanic, and thiocyanic acids.

Thiophosgene, *Thiocarbonyl chloride*, $CSCl_2$. When chlorine is allowed to act upon carbon disulphide, there is first formed the compound $CCl_3 \cdot SCl$, which is converted into thiophosgene by $SnCl_2$. It is a red, mobile, strongly fuming liquid of sweetish taste, which attacks the mucous membrane, and boils at 73°. In its chemical behaviour it closely resembles phosgene, but is much more stable towards water than the latter, being only slowly decomposed even by hot water. With ammonia it yields ammonium thiocyanate and not thiocarbamide.

Thiocarbonic Acids.—Tri-thiocarbonic acid is made up of the constituents $CS_2 + H_2S$, so that carbon disulphide is its thio-anhydride, while the di-thiocarbonic acids contain the elements of $CS_2 + H_2O$ or of $COS + H_2S$, and the mono-acids those of $COS + H_2O$ or of $CO_2 + H_2S$. We find accordingly that CS_2 combines with Na_2S to CS_3Na_2, sodium tri-thiocarbonate, with KSC_2H_5 to $CS(SC_2H_5)SK$, with KOC_2H_5 (*i.e.* an alcoholic solution of potash) to $CS(OC_2H_5)SK$, potassium xanthate. In a similar manner COS and $CSCl_2$ combine with mercaptides and alcoholates.

Tri-thiocarbonic acid, CS_3H_2, is a brown oil, insoluble in water, and readily decomposed, and its **ethyl ester**, $S:C(SC_2H_5)_2$, a liquid boiling at 240°.

Potassium xanthate, $S:C\!\begin{matrix}\diagup OC_2H_5\\ \diagdown SK\end{matrix}$, obtained by the action of potassium ethoxide, $(KOH + C_2H_5OH)$, on carbon disulphide,

crystallizes in beautiful colourless needles, very readily soluble in water, less so in alcohol. A solution of cupric sulphate throws down cupric xanthate as a yellow unstable precipitate, hence the name. It is employed in indigo printing. The free **xanthic acid,** or ethyl hydrogen di-thiocarbonate, $CS(OC_2H_5)SH$, is an oil insoluble in water, and decomposes at so low a temperature as 25° into carbon disulphide and alcohol.

Thiocarbamic Acids.—Di-thiocarbamic acid, $NH_2\cdot CS\cdot SH$, is formed as ammonium salt by the combination of CS_2 and NH_3 in alcoholic solution: $CS_2 + 2\,NH_3 = NH_2\cdot CS\cdot SNH_4$. The free acid is a reddish oil which easily decomposes into thiocyanic acid and sulphuretted hydrogen:



$$NH_2\cdot CS\cdot SH = CSNH + SH_2.$$

Carbon disulphide combines in an analogous manner with primary amines to form the amine salts of alkylated di-thiocarbamic acids; thus ethylamine yields **ethylamine ethyl-di-thiocarbamate,** $C_2H_5NH\cdot CS\cdot SNH_3C_2H_5$. When such salts are heated above 100°, H_2S is evolved and a dialkyl-thiourea left behind, *e.g.* **diethyl-thio-urea,** $CS(NHC_2H_5)_2$; when $HgCl_2$ or $AgNO_3$ is added to their solutions, the Hg or Ag salts of the acids are precipitated, and these decompose on boiling with water into HgS or Ag_2S and the corresponding mustard oil (cf. p. 285):

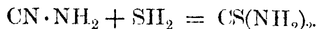


$$2\,CS(NHC_2H_5)\cdot SAg = 2\,CSNC_2H_5 + Ag_2S + H_2S.$$

Secondary amines also give rise to alkylated di-thiocarbamic acids, but the latter do not yield mustard oils.

Thiocarbamide, *Thio-urea, sulpho-urea,* $S:C(NH_2)_2$ (*Reynolds*), is the analogue of urea, and its *modes of formation* are exactly similar to those of the latter. Thus it is formed from ammonium thiocyanate just as urea is from the cyanate.

To effect this molecular transformation a temperature of at least 130° is required, and it is only partial, as the reaction is reversible. At 170° equilibrium is attained after 45 minutes, and the mixture then contains only 25 per cent of thiocarbamide (*Reynolds* and *Werner*, P. 1902, 207). It may also be formed by the direct union of sulphuretted hydrogen with cyanamide:



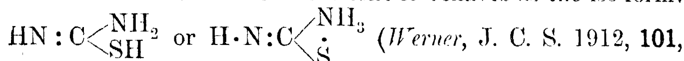
$$CN\cdot NH_2 + SH_2 = CS(NH_2)_2.$$

Thiocarbamide crystallizes in rhombic six-sided prisms, or—if not quite pure—in long silky needles, readily soluble in

water and alcohol. M.-pt. 172°. It is easily hydrolysed to CO_2, H_2S, and $2\,NH_3$. HgO abstracts H_2S from it, with formation of cyanamide. Cold permanganate of potash solution oxidizes it to urea. As a weak base it forms salts with strong acids, but also yields salts with HgO and other metallic oxides; it also combines with salts, such as AgCl, $PtCl_4$, &c. When heated with alcoholic potash to 100°, it is reconverted into (the potassium salt of) thiocyanic acid and ammonia.

Thiocarbamide gives rise to alkyl derivatives (normal and pseudo), acyl derivatives, cyclic ureides, &c., in much the same manner as urea itself.

In most of its chemical reactions it behaves as the iso-form:

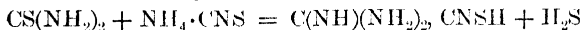


$HN:C\langle^{NH_2}_{SH}$ or $H\cdot N:C\langle^{NH_3}_{\dot{S}}$ (*Werner*, J. C. S. 1912, **101**, 1167, 1982, 2116, 2180). With monochloracetic acid it yields $NH:C(NH_2)\cdot S\cdot CH_2\cdot CO_2H$ (*ibid.* 1914, **105**, 2159; J. A. C. S. 1914, **36**, 364).

E. Amidines of Carbonic Acid

Guanidine, or **Imino-carbamide,** $NH:C(NH_2)_2$, (*Strecker*, 1861), may be obtained by the oxidation of guanine, also by heating cyanamide and ammonium iodide, and therefore from cyanogen iodide and ammonia, $CN\cdot NH_2 + NH_4I = CN_3H_5, HI$.

It is usually prepared as isothiocyanate by heating thio-urea with ammonium thiocyanate to 180°–190° (*Volhard*):



$$CS(NH_2)_2 + NH_4\cdot CNS = C(NH)(NH_2)_2, CNSH + H_2S$$

The perchlorate is formed by the action of ammonium perchlorate on dicyanodiamide. Alkylated guanidines are formed by the action of an alkylamine hydrochloride on dicyanodiamide, $C_2H_4N_4$, *Werner* and *Bell* (J. C. S., 1922, 1790.)

Guanidine crystallizes well, is readily soluble in water and alcohol, deliquesces in the air, and is a sufficiently strong monoacid base to absorb carbon dioxide. **Guanidine carbonate,** $(CN_3H_5)_2, H_2CO_3$, crystallizes beautifully in quadratic prisms. The base is readily hydrolysed, at first to urea and ammonia, and finally to ammonia and carbon dioxide.

By the action of a mixture of nitric and sulphuric acids upon guanidine nitrate, **nitro-guanidine,** $NH_2\cdot C(NH)NH\cdot NO_2$, is obtained, which is readily reduced to **amino-guanidine,** $NH_2\cdot C(NH)NH\cdot NH_2$. The latter, when boiled with alkalis or acids, breaks up into *hydrazine*, N_2H_4, ammonia, and carbon

dioxide, and it yields with nitrous acid **diazo-guanidine**, $NH_2C(NH)NHN:N \cdot OH$, which in its turn is decomposed by alkalis into water, cyanamide, and *hydrazoic acid*, N_3H (*Curtius*, A. 1900, **314**, 339).

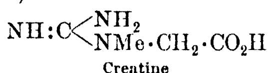
By the direct combination of cyanamide with glycocoll there is formed **glycocyamine**:



which readily loses water with formation of **glycocyamidine**:



If, instead of glycocoll, its methyl derivative, sarcosine, is used, we obtain in an analogous manner creatine and creatinine (*Volhard*):



Creatine



Creatinine.

Creatine is present in the juice of muscle, and is prepared from extract of meat (*Liebig*). It crystallizes in neutral prisms ($+ H_2O$) of a bitter taste, is moderately soluble in hot water, but only slightly in alcohol. When heated with acids it loses water and yields **creatinine**, which is an invariable constituent of urine, and which forms a characteristic double salt with zinc chloride, $2C_4H_7N_3O + ZnCl_2$. It is a strong base and much more readily soluble than creatine.

Creatinine is the methyl derivative of imino-hydantoïn, and as such yields, when carefully hydrolysed, ammonia and methyl-hydantoïn.

XIV. CARBOHYDRATES

Most of the carbohydrates which occur in nature have been known for a long time. Cane-sugar was found in the sugar-beet by *Marggraf* in 1747, and dextrose in honey by *Glauber*. The transformation of starch into glucose (p. 321) was first observed by *Kirchoff* in 1811.

The name **carbohydrate** was formerly applied to certain substances which occur naturally in large quantities in the vegetable and animal kingdom, and which could be repre-

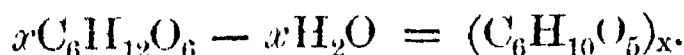
sented by the general formula $C_x(H_2O)_y$, where $x = 6$ or a multiple of 6, *e.g.* dextrose, $C_6(H_2O)_6$ or $C_6H_{12}O_6$, cane-sugar, $C_{12}(H_2O)_{11}$ or $C_{12}H_{22}O_{11}$, and starch $[C_6(H_2O)_5]_x$. In addition to these natural products, the group at the present time includes a number of compounds which have only been obtained synthetically, mainly as a result of the researches of *E. Fischer.* The number of carbon atoms in these varies considerably. Carbohydrates are now known in which the hydrogen and oxygen are not present in the proportions of 2 atoms of hydrogen to 1 of oxygen, *e.g.* rhamnose, $C_6H_{12}O_5$.

The carbohydrates are usually divided into the three following groups, according to their relative complexity:—

A. **Monosaccharoses.***—This is the simplest group of the carbohydrates, and the members are all polyhydroxy aldehydes or ketones containing from 3–9 carbon atoms. The group includes the common substances arabinose, $C_5H_{10}O_5$, and the isomeric compounds, $C_6H_{12}O_6$, glucose or grape-sugar, and fructose or fruit-sugar. As a rule, the compounds are readily soluble in water, have a sweet taste, and do not crystallize very readily.

B. **Di-** and **Trisaccharoses.**—These compounds may be regarded as anhydrides of the monoses,† usually derived by the elimination of 1 molecule of water from 2 mols. of the monose, or of 2 mols. of water from 3 of a monose. It is not necessary that the 2 or 3 molecules of monose should be identical in structure, *e.g.* cane-sugar is the anhydride produced by the elimination of 1 mol. of water from 1 mol. of glucose and 1 of fructose. As anhydro derivatives they are readily hydrolysed by mineral acids, yielding the monoses, from which they may be regarded as being derived. Most of the di- and trioses are soluble in water, crystallize very well, and also possess a sweet taste. Examples are cane-sugar, maltose, and milk-sugar.

C. **Polysaccharoses** or **Polyoses.**—This group includes the complex carbohydrates, such as starch, cellulose, &c. They may be regarded as derived from the monoses by the elimination of x mols. of water from x mols. of a monose, *e.g.*:



$$xC_6H_{12}O_6 - xH_2O = (C_6H_{10}O_5)_x.$$

In conformity with such a structure they are fairly readily hydrolysed, yielding as the ultimate product a monose. As a rule, they do not dissolve in water, possess no sweet taste, and have not been obtained in a crystalline form.

* Often called monosaccharides.

† Monose is a contraction for monosaccharose.

A. Monosaccharoses

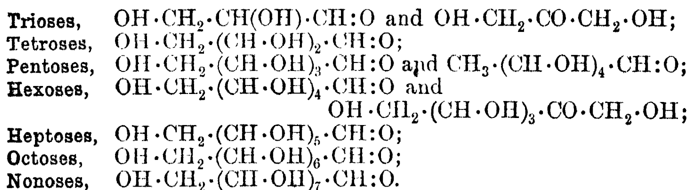
These are all open-chain* polyhydroxy-aldehydes or ketones,



$OH\cdot CH_2\cdot CH(OH)\cdot CH(OH)\cdot CH(OH)\cdot CH{:}O$ Arabinose,
$OH\cdot CH_2\cdot CH(OH)\cdot CH(OH)\cdot CH(OH)\cdot CO\cdot CH_2\cdot OH$ Fructose,

and are divided into the two main groups **aldoses** and **ketoses,** according to their aldehydic or ketonic constitution. As a rule, several hydroxyl groups are present in addition to the aldehydic $\cdot C{<}^{H}_{O}$ or ketonic $>C{:}O$ group, and invariably one of these hydroxyl groups is in the α-position with respect to the aldehydic or ketonic group.

The monosaccharoses are usually divided into sub-groups, according to the number of **oxygen atoms** in the molecule, *e.g.*:

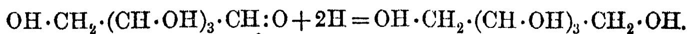


Trioses, $OH\cdot CH_2\cdot CH(OH)\cdot CH{:}O$ and $OH\cdot CH_2\cdot CO\cdot CH_2\cdot OH$;
Tetroses, $OH\cdot CH_2\cdot (CH\cdot OH)_2\cdot CH{:}O$;
Pentoses, $OH\cdot CH_2\cdot (CH\cdot OH)_3\cdot CH{:}O$ and $CH_3\cdot (CH\cdot OH)_4\cdot CH{:}O$;
Hexoses, $OH\cdot CH_2\cdot (CH\cdot OH)_4\cdot CH{:}O$ and $OH\cdot CH_2\cdot (CH\cdot OH)_3\cdot CO\cdot CH_2\cdot OH$;
Heptoses, $OH\cdot CH_2\cdot (CH\cdot OH)_5\cdot CH{:}O$;
Octoses, $OH\cdot CH_2\cdot (CH\cdot OH)_6\cdot CH{:}O$;
Nonoses, $OH\cdot CH_2\cdot (CH\cdot OH)_7\cdot CH{:}O$.

As a rule, the molecule of any single monose contains several asymmetric carbon atoms, *e.g.* a hexose, $OH\cdot CH_2(CH\cdot OH)_4\cdot CH{:}O$, contains 4 asymmetric carbon atoms, and hence should exist in 2^4, *i.e.* sixteen distinct optically active modifications, in addition to eight racemic forms. In most cases all the possible stereo-isomeric modifications are not known, but the number of such compounds known has been largely increased owing to the brilliant researches of *Emil Fischer* (B. 1890, **23**, 2114; 1894, **27**, 3189).

General Characteristics of Aldoses.—As aldehydes the aldoses possess most of the properties already described as characteristic of fatty aldehydes.

They are readily reduced by ordinary alkaline reducing agents, yielding polyhydric alcohols:



$$OH\cdot CH_2\cdot (CH\cdot OH)_3\cdot CH{:}O + 2H = OH\cdot CH_2\cdot (CH\cdot OH)_3\cdot CH_2\cdot OH.$$

* **For ring structure, cf. Chap. XLVIII, C.**

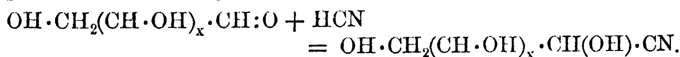
When oxidized, they yield first mono- and then dibasic acids, containing the same number of carbon atoms:



$$OH\cdot CH_2\cdot(CH\cdot OH)_4\cdot CH{:}O \rightarrow OH\cdot CH_2\cdot(CH\cdot OH)_4\cdot CO\cdot OH \rightarrow COOH\cdot(CH\cdot OH)_4\cdot COOH.$$

These reactions are of considerable importance as direct evidence of the aldehydic nature of the aldoses. The first stage of the oxidation is effected by mild oxidizing agents, such as chlorine, bromine water especially in presence of calcium benzoate, silver oxide, or ammoniacal solutions of cupric salts. The last-mentioned reaction is the basis of the usual volumetric method for the estimation of glucose and other aldoses. The aldose solution is added to a given volume of a standard *Fehling's* solution (a solution containing cupric sulphate, sodium ammonium tartrate, and caustic soda (p. 262)) until the blue colour just disappears on boiling. An even more exact method is to weigh the cuprous oxide (as such, as metallic copper, or as cupric oxide) formed by reducing a given volume of the sugar solution with an excess of *Fehling's* solution. The oxidation to a dibasic acid requires somewhat stronger oxidizing agents, *e.g.* nitric acid. With nitric acid in the absence of air a keto-monobasic acid can be formed, *e.g.* from glucose an acid $OH\cdot CH_2\cdot(CH\cdot OH)_3\cdot CO\cdot CO_2H$. *Kiliani* (B. 1922, 493).

Although the aldoses do not combine directly with ammonia or sodium hydrogen sulphite, they readily form additive compounds with hydrogen cyanide (cf. p. 313):

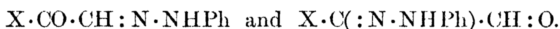


$$OH\cdot CH_2(CH\cdot OH)_x\cdot CH{:}O + HCN = OH\cdot CH_2(CH\cdot OH)_x\cdot CH(OH)\cdot CN.$$

They react normally with hydroxylamine especially in alcoholic solution, yielding **oximes**, which can be converted into monoses containing a smaller number of oxygen atoms (p. 316).

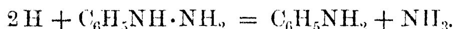
They can also react normally with phenyl-hydrazine, yielding **phenyl-hydrazones**, which, as a rule, are sparingly soluble, colourless, crystalline compounds with definite melting-points. These are readily transformed back into the aldoses by treatment with hydrolysing agents or with benzaldehyde (A. 1895, **288**, 140). Substituted phenyl-hydrazines, *e.g.* the *p*-bromophenyl- or diphenyl-hydrazine, are frequently used for isolating and characterizing sugars. One of the most characteristic properties of monoses is the formation of **osazones** or **diphenylhydrazones**. This reaction may be regarded as taking place in three distinct stages:—(*a*) Formation of a phenyl-hydrazone,

$X \cdot CH(OH) \cdot CH:N \cdot NHPh$, in the case of an aldose, and $X \cdot C(:N \cdot NHPh) \cdot CH_2 \cdot OH$ in the case of a ketose; (*b*) the oxidation of the $>CH \cdot OH$ or $\cdot CH_2 \cdot OH$ group in the α-position with regard to the carbon atom to which the hydrazino-group is attached and the formation of a $>CO$ or $\cdot CH:O$ group, *e.g.*:



$$X \cdot CO \cdot CH:N \cdot NHPh \text{ and } X \cdot C(:N \cdot NHPh) \cdot CH:O.$$

This oxidation occurs at the expense of the excess of phenyl-hydrazine, which becomes reduced to aniline and ammonia:

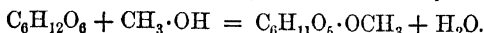


$$2H + C_6H_5NH \cdot NH_2 = C_6H_5NH_2 + NH_3.$$

(*c*) The compounds thus obtained react with a further quantity of phenyl-hydrazine, so that a second hydrazino-group is introduced, *e.g.* $X \cdot C(:N \cdot NHPh) \cdot CH:N \cdot NHPh$, and an osazone formed (*E. Fischer*). From the above formulæ it is clear that the same osazone can be obtained from a ketose and an isomeric aldose (cf. Glucose and Fructose). These osazones are usually prepared by warming a dilute acetic acid solution of phenyl-hydrazine with the sugar for an hour or more on the water-bath. The products are yellow crystalline solids with definite melting-points; they are only sparingly soluble, and are largely made use of for characterizing the various monoses. Methyl-phenyl-hydrazine, $NMePh \cdot NH_2$, yields osazones with ketoses, but not with aldoses, and this difference is made use of in the separation of the two groups of compounds (B. 1902, **35**, 3141). The complex hydrazine di-methyl-hydrazino-di-phenyl-methane, $CH_2(C_6H_4 \cdot NMe \cdot NH_2)_2$, is often used in connection with aldoses, as both NH_2 groups react, giving crystalline compounds when two of the $CH \cdot OH$ groups adjacent to the CHO group have the same spatial arrangement.

The hydroxylic nature of the aldoses can be established in various ways. Like all alcohols, they contain hydrogen atoms which can be replaced by metallic radicals. This replacement can be accomplished not only by means of metals themselves (cf. action of sodium on ethyl alcohol), but much more conveniently by means of the metallic hydroxides. The most common derivatives are the calcium, barium, or plumbous; thus from glucose, $C_6H_{12}O_6$, **calcium glucosate**, $C_6H_{11}O_6 \cdot Ca \cdot OH$, is readily obtained. Many of these metallic derivatives are sparingly soluble, and are therefore made use of in the isolation of certain sugars. They are readily transformed into the original sugar when decomposed by carbon dioxide in aqueous solution.

As alcohols the aldoses also give rise to ethers; the best known are the mono-methyl ethers of glucose, *i.e.* mixed ethers derived from the two alcohols, glucose and methyl alcohol:



$$C_6H_{12}O_6 + CH_3{\cdot}OH = C_6H_{11}O_5{\cdot}OCH_3 + H_2O.$$

These compounds are usually spoken of as **glucosides,** and are probably closely related to the natural glucosides (Chap. XLII, B.). They may be obtained readily by the action of dry hydrogen chloride on a methyl alcoholic solution of glucose (*E. Fischer*, B. 1894, **28**, 1151). (See also Chap. XLVIII, B.)

Completely methylated derivatives of the monosaccharoses are obtained by taking the mono-methyl ethers and alkylating with methyl sulphate and sodium hydroxide. In this way **pentamethyl** derivatives, $C_6H_7O(OMe)_5$, are obtained (*Haworth*, J. C. S. 1915, **107**, 8).

The formation of **acetyl** derivatives is also a direct proof of the presence of hydroxyl radicals in the aldose molecules. Thus glucose when heated with acetic anhydride and anhydrous sodium acetate yields a pentacetate or **pentacetyl** derivative, which can be hydrolysed to acetic acid and glucose.

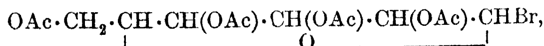
They also form well defined condensation products with acetone cf. Chap. XLVIII, C.

Partially alkylated and acylated aldoses have been prepared; one of the common methods is to condense the aldose with acetone in the presence of a little hydrogen chloride (*Irvine* and *Macdonald*, *ibid.*, 1706), then to alkylate or acylate, and finally to hydrolyse with mild hydrolytic reagents, so as to remove the acetone but to leave the alkyl or acyl groups intact (*Purdie* and *Young*, J. C. S. 1906, **89**, 1194; *Irvine* and *Scott*, *ibid.*, 1913, **103**, 564, 575; *E. Fischer*, B. 1915, **48**, 266; 1916, **49**, 88). Thus:

Glucose-mono-acetone yields → tri-methyl glucose.
→ tri-benzyl glucose.

Glucose-di-acetone yields mono-methyl glucose.

Important acyl derivatives are those of the type of **tetra-acetobromoglucose:**

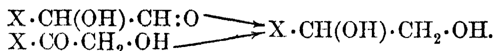


$$OAc{\cdot}CH_2{\cdot}\underbrace{CH{\cdot}CH(OAc){\cdot}CH(OAc){\cdot}CH(OAc){\cdot}CHBr}_{O},$$

which contain a reactive bromine atom, and are hence of great value as synthetical reagents (cf. Chap. XLII, B.).

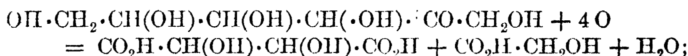
General Characteristics of Ketoses.—In the majority of their properties the ketoses resemble the aldoses, *e.g.* they

react with hydroxylamine and phenyl-hydrazine in exactly the same manner. They form additive compounds with hydrogen cyanide, and are readily reduced to polyhydric alcohols. In certain cases the same alcohol is obtained by the reduction of a ketose and of an isomeric aldose, *e.g.* both *d*-glucose and *d*-fructose yield *d*-sorbitol on reduction:



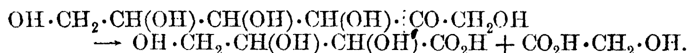
$$\begin{matrix} X\cdot CH(OH)\cdot CH{:}O \\ X\cdot CO\cdot CH_2\cdot OH \end{matrix} \rightarrow X\cdot CH(OH)\cdot CH_2\cdot OH.$$

The ketoses differ completely from the aldoses as regards their oxidation products. As ketones they do not yield mono- or dibasic acids containing the *same number of carbon atoms*,* but always a mixture of simpler acids, *e.g.* *d*-fructose on oxidation with nitric acid yields a mixture of tartaric and glycollic acids:



$$OH\cdot CH_2\cdot CH(OH)\cdot CH(OH)\cdot CH(\cdot OH)\cdot \vdots CO\cdot CH_2OH + 4\,O$$
$$= CO_2H\cdot CH(OH)\cdot CH(OH)\cdot CO_2H + CO_2H\cdot CH_2OH + H_2O;$$

or when boiled with mercuric oxide it yields glycollic and trihydroxy-butyric acids:



$$OH\cdot CH_2\cdot CH(OH)\cdot CH(OH)\cdot CH(OH)\cdot \vdots CO\cdot CH_2OH$$
$$\rightarrow OH\cdot CH_2\cdot CH(OH)\cdot CH(OH)\cdot CO_2H + CO_2H\cdot CH_2\cdot OH.$$

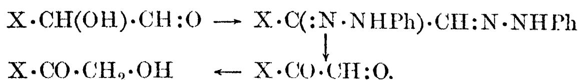
The ketoses also form metallic derivatives and acetyl derivatives.

Alcoholic Fermentation of Monosaccharoses.—Many of the natural products, *e.g.* *d*-glucose and *d*-fructose, are readily fermented by yeast (*Saccharomyces*), yielding as chief products ethyl alcohol and carbon dioxide (p. 79). This decomposition is undoubtedly due to the presence of an enzyme, *Buchner's* **zymase**, which is contained in the cells of the organism. *Fischer's* researches have shown that all monoses cannot be fermented, only certain of those containing 3 or a multiple of 3 carbon atoms. Even such monoses are not all readily fermented, *e.g.* *d*-glucose is fermented more readily than *l*-glucose, and the isomeric guloses cannot be fermented by yeast. There appears to be an intimate relationship between the configuration of the monose molecule and of the ferment (enzyme) which is capable of decomposing it. *Fischer* has compared this relationship to that of a lock and its corresponding key.

Conversion of an Aldose into an Isomeric Ketose.—This

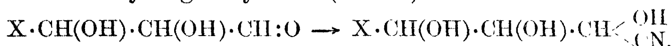
* The formation of acids containing the same number of carbon atoms is theoretically possible, since two $\cdot CH_2\cdot OH$ groups are present, but such acids have not been obtained.

is an interesting transformation due to *E. Fischer*, and consists in converting the aldose into its osazone, which on hydrolysis with hydrochloric acid yields phenyl-hydrazine and a poly-hydroxy-ketonic aldehyde, usually known as an **osone**. When the osone is reduced, the aldehydo-group is converted into a primary alcoholic radical, and a hydroxy-ketone (ketose) isomeric with the original aldose is obtained, *e.g.*:

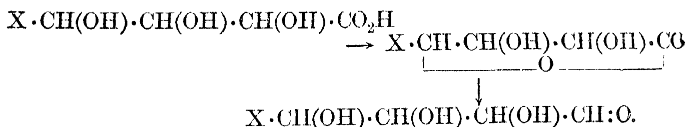


By this means *d*-glucose can be transformed into *d*-fructose.

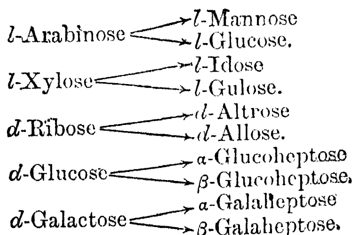
Synthesis of a Monosaccharose from a Simpler Monosaccharose.—The aldose is converted into its cyanhydrin by means of hydrogen cyanide (*Kiliani*):



As this reaction involves the introduction of a further asymmetric carbon atom into the molecule, two distinct optically active nitriles will be formed. As the two compounds are not related to one another as object to mirror image, they will not be optical antipodes, and will not necessarily be formed in equal amount. The mixture of cyanides is hydrolysed, the resulting hydroxy acids converted into **lactones** and then reduced with sodium amalgam, when a mixture of two sugars is obtained:

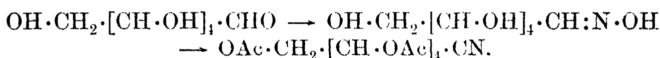


As examples of this we have:



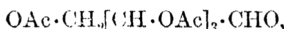
By similar methods *E. Fischer* has succeeded in preparing **octoses** and **nonoses.** For configuration of the latter, see *Pierce*, J. Biol. C. 1915, **23**, 327. Two heptoses have been isolated from natural products, viz. a **mannoketoheptose**, from Avogadro pear (Abs. 1917, i, 118), and **sedoheptose**, from the leaves and stems of *Sedum spectabile*.

Conversion of a Monosaccharose into a Simpler Monosaccharose (*Wohl*, B. 1893, **26**, 730).—1. The aldose is converted into its oxime, which reacts with acetic anhydride, yielding an acetylated hydroxy-nitrile, *e.g.*:



$$OH\cdot CH_2\cdot[CH\cdot OH]_4\cdot CHO \longrightarrow OH\cdot CH_2\cdot[CH\cdot OH]_4\cdot CH{:}N\cdot OH \longrightarrow OAc\cdot CH_2\cdot[CH\cdot OAc]_4\cdot CN.$$

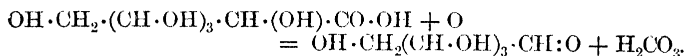
The nitrile when treated with ammoniacal silver nitrate solution loses hydrogen cyanide and yields the acetyl derivative of a lower monose, *e.g.*:



$$OAc\cdot CH_2[CH\cdot OAc]_3\cdot CHO,$$

from which the monose itself is readily obtained.

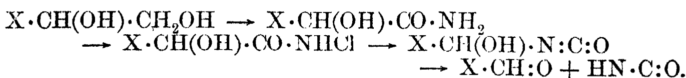
2. Another method worked out by *Ruff* (B. 1898, **31**, 1573; 1900, **33**, 1798; 1902, **35**, 2360) consists in oxidizing the aldose to the corresponding monobasic acid, and then oxidizing the calcium salt of this with ferric acetate and hydrogen peroxide. Carbonic acid is split off and an aldose obtained:



$$OH\cdot CH_2\cdot(CH\cdot OH)_3\cdot CH\cdot(OH)\cdot CO\cdot OH + O = OH\cdot CH_2(CH\cdot OH)_3\cdot CH{:}O + H_2CO_3.$$

The aldose can be isolated as its phenylhydrazone, and this with benzaldehyde yields the free aldose.

3. A third method consists in oxidizing to the lactone of the monobasic acid, preparing the amide of the acid by the addition of ammonia to the lactone and the action of hypochlorous on the amide (*Hofmann* reaction, p. 191):



$$X\cdot CH(OH)\cdot CH_2OH \longrightarrow X\cdot CH(OH)\cdot CO\cdot NH_2 \longrightarrow X\cdot CH(OH)\cdot CO\cdot NHCl \longrightarrow X\cdot CH(OH)\cdot N{:}C{:}O \longrightarrow X\cdot CH{:}O + HN\cdot C{:}O.$$

In this way *d*-glucose yields *d*-arabinose and *d*-galactose *d*-lyxose (*Warman*, Abs. 1915, **i**, 387; 1917, **i**, 546).

Trioses.—When glycerol is oxidized with dilute nitric acid or other oxidizing agents, a product $C_3H_6O_3$ is obtained, which

has been termed **glycerose**. This has been shown to consist of the ketone, dihydroxyacetone, $OH \cdot CH_2 \cdot CO \cdot CH_2 \cdot OH$, with a small amount of the isomeric aldehyde, glyceraldehyde, $OH \cdot CH_2 \cdot CH(OH) \cdot CH:O$,* and may be regarded as the simplest monose. It is a syrup, possesses most of the characteristic properties of the monoses, and when warmed with alkalis undergoes condensation and yields a hexose (*a*-acrose) (p. 325) which closely resembles fructose.

Tetroses, $C_4H_8O_4$.—A tetrose, **erythrose**, can be obtained by the oxidation of erythritol, $OH \cdot CH_2[CH \cdot OH]_2 \cdot CH_2 \cdot OH$, with nitric acid, and is probably a mixture of an aldose and ketose. Other tetroses can be obtained from the pentoses by the general methods described on p. 316.

Pentoses.—The pentoses are characterized by the fact that they yield furfuraldehyde or methyl-furfuraldehyde upon prolonged boiling with hydrochloric acid, water being eliminated. This reaction is largely made use of for their quantitative estimation (B. 1892, **25**, 2912; 1898, **30**, 2570). Arabinose gives furfuraldehyde itself, while its homologue, rhamnose, gives methyl-furfuraldehyde. When warmed with hydrochloric acid and phloroglucinol, cherry-red colorations are produced. The pentoses do not appear to exist free in the animal or vegetable kingdom, but are readily formed by the hydrolysis of various natural gummy carbohydrates.

l-**Arabinose**, $C_5H_{10}O_5 = OH \cdot CH_2 \cdot [CH \cdot OH]_3 \cdot CH:O$, is produced by boiling gum-arabic, cherry gum, or beet-root chips with dilute sulphuric acid, and forms prisms which dissolve in water to a dextro-rotatory solution. It combines with hydrogen cyanide, and thus yields the nitriles of two stereo-isomeric hydroxy-caproic acids, viz. *l*-mannonic acid (*Kiliani*, B. **20**, 339, 1233) and *l*-gluconic acid (*E. Fischer*). In addition to *l*-arabinose, a *d*-arabinose and a *d*-*l*- or racemic arabinose are also known. They are related to one another in exactly the same manner as *l*-, *d*-, and *r*-tartaric acid. The corresponding alcohol is arabitol.

l-**Xylose**, or *Wood-sugar*, is stereo-isomeric with arabinose, and is prepared by boiling wood-gum, straw, and jute with dilute sulphuric acid, and is very similar to arabinose. (For its constitution, see B. **24**, 537.) The corresponding alcohol is xylitol. **Ribose** (B. 1891, **24**, 4214) and **Lyxose** (B. 1899, **33**, 1798; J. C. S. 1928, 1221) are stereo-isomeric with arabinose.

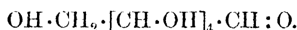
* For preparation of glyceraldehyde, cf. J. A. C. S. 1914, **36**, 2223.

Rhamnose, or *Isodulcite*, $C_6H_{12}O_5$, = $CH_3 \cdot [CH \cdot OH]_4 \cdot CH:O$, is obtained from several glucosides, *e.g.* quercitrin or xanthorhamnin (yellow needles, present in French berries, *Rhamnus tinctoria*, &c.), by the action of dilute sulphuric acid. It forms colourless crystals which contain 1 H_2O, melts at 93°, and distilled with sulphuric acid yields α-methyl-furfuraldehyde.

Several isomerides of rhamnose are known, *e.g.* **fucose** from sea-weed, **epifucose, quinovose, rhodeose** and **isorhamnose.**

Hexoses.—The hexoses constitute the most important group, as they contain all the more common natural monosaccharoses, *e.g.* *d*-glucose, *d*-fructose, *d*-galactose, &c. These occur in the free state in the juices of ripe fruits, and are also found combined with acids and other compounds in the ether- or ester-like compounds known as glucosides. They are also formed by the hydrolysis of more complex carbohydrates, *e.g.* cane-sugar, maltose, milk-sugar, or starch, either under the influence of mineral acids or of enzymes. They are sweet, and for the most part crystalline compounds readily soluble in water, sparingly in absolute alcohol, and insoluble in ether. They possess the chemical properties of pentahydroxy-aldehydes and ketones.

Aldohexoses.—The common aldohexoses have the constitution represented by the formula:



$$OH \cdot CH_2 \cdot [CH \cdot OH]_4 \cdot CH:O.$$

In this formula the 4 carbon atoms contained within the brackets are asymmetric carbon atoms, and hence such a compound should exist in numerous stereo-isomeric forms. It can be shown that in this case the number of optically active isomerides theoretically possible is sixteen; of these some thirteen are actually known, namely:

Aldohexose.	Monobasic Acid.	Dibasic Acid, $CO_2H[CH \cdot OH]_4 \cdot CO_2H$.	Alcohol.	M.-p. of Osazone.
d- & *l*-Mannose	*d*- & *l*-Mannonic acid	*d*- & *l*-Mannosaccharic	*d*- & *l*-Mannitol	206°
d- & *l*-Glucose	*d*- & *l* Gluconic acid	*d*- & *l*-Saccharic	*d*- & *l*-Sorbitol	Ibid
d- & *l*-Gulose	*d*- & *l*-Gulonic acid	*d*- & *l*-Saccharic	*d*- & *l*-Sorbitol	156°
d- & *l*-Idose	*d*- & *l*-Idonic acid	*d*- & *l*-Idosaccharic	*d*- & *l*-Iditol	156°
d- & *l*-Galactose	*d*- & *l*-Galactonic acid	*i*-Mucic	*i*-Dulcitol	206°
d-Talose	*d*-Talonic acid	*d*-Talomucic	*d*-Talitol	188°
d-Altrose	*d*-Altronic acid	*d*-Talomucic	—	183–185°
d-Allose	*d*-Allonic acid	Allomucic	—	183–185°

All of these hexoses have to be represented by the same structural formula, and only differ as regards the spatial arrangements of the various radicals within the molecule. All are optically active in solution, and the majority form

pairs of optical antipodes, *e.g.* *d*- and *l*-glucose, which are related in exactly the same manner as *d*- and *l*-tartaric acids. The members of such a pair are identical as regards their ordinary chemical and physical properties, with the exception of their effects on polarized light, and their behaviour towards enzymes or ferments generally. As a rule, one of the two compounds exists naturally, *e.g.* *d*-glucose, and the second must be prepared by artificial means. The two are able to form a racemic compound, which differs as regards its physical properties from the active components.

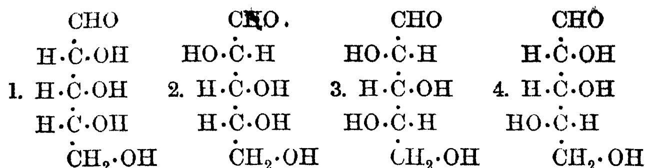
The determination of the configuration of each aldohexose has been accomplished by *E. Fischer* largely from a study of the following points:—(*a*) The relationship of the aldohexose to the aldopentoses, *e.g.* *l*-arabinose can be transformed into a mixture of *l*-glucose and *l*-mannose, and hence in all three compounds the configuration of the following part of the molecule—$OH \cdot CH_2 \cdot CH(OH) \cdot CH(OH) \cdot CH(OH)$—must be identical. (*b*) The nature of the dibasic acid formed on oxidation, or of the alcohol formed on reduction. When reduced, *d*-galactose yields an inactive hexahydric alcohol, viz. *i*-dulcitol, and from this it follows that in the *d*-galactose molecule the H and OH radicals must be so spatially arranged that when the $\cdot CH{:}O$ group is converted into a $CH_2 \cdot OH$ group a symmetrical molecule is obtained (see formula below). (*c*) The nature of the osazone; *e.g.* *d*-glucose and *d*-mannose both give rise to the same osazone—*d*-glucosazone—and hence the spatial arrangements of the two molecules must be identical, with the exception of the part $\cdot CH(OH) \cdot CH{:}O$.

As the result of such methods, the configurations given on p. 320 have been arrived at for some of the commoner aldohexoses (B. 1891, **24**, 2683; 1894, **27**, 3211).

The actual positions of H and OH are often determined by conversion into *d*- or *l*-tartaric acid (p. 261). Thus *d*-glucose → *d*-saccharic acid → *d*-tartaric acid, establishes the positions of the OH and H groups attached to C atoms 2 and 3, but *d*-saccharamide with bromine and alkali gives *l*-tartaric acid, and thus the position of H and OH groups attached to C atoms 3 and 4 (formula p. 320). (*Bergmann*, B. 1921, 2651).

A clearer conception of the manner in which such arguments are used can be gathered by a study of the aldopentoses. Eight active forms are theoretically possible, and the *d*- and *l*- forms of arabinose, xylose, lyxose, and ribose are the compounds actually known. The possible configura-

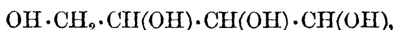
tions are the four given below and their enantiomorphs:



Since arabinose and ribose give the same osazone they must be either 1 and 2 or 3 and 4. Arabinose on oxidation gives an optically active trihydroxyglutaric acid, hence arabinose can only have the configuration 2 or 4. Further, arabinose with hydrogen cyanide and subsequent hydrolysis and oxidation gives two *active* dicarboxylic acids, and must therefore have the structure 2, as one of the acids derived in this way from 4 would be optically inactive by internal compensation. If 2 represents *d*-arabinose, then its enantiomorph represents *l*-arabinose. As No. 2 represents *d*-arabinose, No. 1 must represent *d*-ribose.

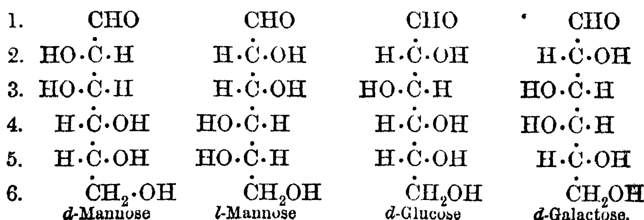
As xylose yields an inactive trihydroxyglutaric acid when oxidized, it must be represented by configuration No. 3, and hence lyxose is No. 4.

Since *d*-arabinose when treated with hydrogen cyanide and the product hydrolysed and reduced yields a mixture of *g*-glucose and *d*-mannose, it follows that in these two latter the spatial arrangements in the portion,



$$OH\cdot CH_2\cdot CH(OH)\cdot CH(OH)\cdot CH(OH),$$

must be identical, as shown in the constitutional formulæ given below:



E. Fischer has suggested the following system of nomenclature. According to the Geneva Congress, the name for

glucose is hexanepentolal. *Fischer* suggests that the asymmetric carbon atoms be numbered with respect to the CHO group, and that when the H is to the left and OH to the right of an asymmetric carbon atom, it is termed + and the reverse −. Thus:

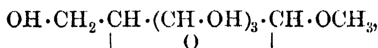
d-Glucose is hexanepentolal,		+ − + +
l-Glucose	„	− + − −
d-Mannose	„	− − + +
d-Galactose	„	+ − − +
d-Gulose	„	− − + −
d-Idose	„	+ − + −
d-Talose	„	− − − +
d-Altrose	„	− + + +
d-Allose	„	+ + + +

d-**Glucose,** *Grape-sugar* or *dextrose,* $C_6H_{12}O_6 + H_2O$, occurs together with *d*-fructose in most sweet fruits, in honey, also diabetic urine. It is prepared by the hydrolysis of more complex carbohydrates, *e.g.* sucrose or starch. The usual method, the hydrolysis of starch with dilute sulphuric acid, yields a product which contains, in addition to dextrose, dextrine and unfermentable substances. It crystallizes from water in nodular masses made up of six-sided plates which melt at 86°, and from methyl alcohol in small anhydrous prisms free from water; m.-pt. 146°. It is dextro-rotatory, $[\alpha]_D = 52{\cdot}6°$, hence the name "dextrose".

A freshly-prepared solution turns the plane of polarization almost twice as much as one which has been kept or heated to boiling, a phenomenon which is known as "bi-, multi-, or muta-rotation". (Cf. Chap. XLVII, I. Physical Constants and Constitution.) The strength of a solution of glucose is usually determined polarimetrically from its specific rotatory power, or gravimetrically by determining the weight of cuprous oxide obtained by the reduction of *Fehling's* solution with a given volume of the solution (cf. p. 311).

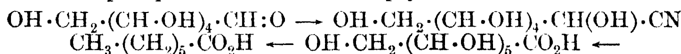
d-**Glucose-phenyl-hydrazone,** $C_{12}H_{18}O_5N_2$, forms fine crystals which melt at 115°. Another modification melts at 144°. *d*-**Phenyl-glucosazone** crystallizes in sparingly soluble needles. The rotation produced by the hydrazones and osazones may be the opposite of that of the mother substance. It is an important point for the recognition of the latter. *d*-**Pentacetyl-glucose,** $C_6H_7O(OC_2H_3O)_5$, melts at 111°. *d*-**Glucosone,** $CH_2(OH)\cdot[CH(OH)]_3\cdot CO\cdot CHO$, forms a syrup which does not ferment with beer yeast, and which yields

the osazone immediately with phenyl-hydrazine. **Methyl glucoside,**


$$OH\cdot CH_2\cdot CH\cdot(CH\cdot OH)_3\cdot CH\cdot OCH_3,$$

exists in two pairs of stereo-isomeric modifications, the *a* compound melts at 165° and the *β* at 107°. *l*-**Glucose** resembles *d*-glucose closely, excepting that it turns the plane of polarization as strongly to the left as the latter does to the right. *i*-**Glucose**, from *i*-gluconic acid, is a colourless syrup. The osazone, *i*-**glucosazone**, melts at 216°, and, apart from rotatory power, is deceptively like the *d*- and *l*-osazones.

Constitution of *d*-Glucose.—Its constitution as a pentahydroxy aldehyde follows from the formation of a pentacetyl derivative, and from its oxidation first to a monobasic acid (gluconic acid) and then to a dibasic acid (saccharic acid), both of which contain the same number of carbon atoms as glucose. A proof both of its aldehydic nature and of the normal structure was afforded by *Kiliani* (B. 1886, **19**, 767), who prepared the cyanhydrin, hydrolysed this to the hexahydroxy-carboxylic acid, and, by reducing this with hydriodic acid and phosphorus, obtained *n*-heptylic acid:


$$OH\cdot CH_2\cdot(CH\cdot OH)_4\cdot CH{:}O \longrightarrow OH\cdot CH_2\cdot(CH\cdot OH)_4\cdot CH(OH)\cdot CN$$
$$CH_3\cdot(CH_2)_5\cdot CO_2H \longleftarrow OH\cdot CH_2\cdot(CH\cdot OH)_5\cdot CO_2H \longleftarrow$$

a product which could not have been formed if the glucose had possessed either a ketonic structure or an iso-chain (cf. Fructose). (For configuration, see p. 320, also Chap. XLVIII C.)

d-**Mannose** is stereo-isomeric with *d*-glucose, and is formed together with *d*-fructose by the cautious oxidation of mannitol, also by boiling the reserve cellulose of the seed of the Brazil-nut (*Bertholletia excelsa*), or of the seeds of the Ivory-palm (*Phytelephas macrocarpa*), with dilute mineral acid, and by reducing mannonic acid lactone with sodium amalgam. It forms colourless crystals readily soluble in water, is dextrorotatory, $[a]_D = +14{\cdot}36°$, and yields the same osazone as *d*-glucose. When treated with sodium amalgam it passes readily into *d*-mannitol. The **hydrazone** melts at 195°, and is sparingly soluble in water. *i*-**Mannose** forms a colourless syrup. The osazone is identical with that from *i*-fructose. *l*-**Mannose** is not so readily fermented as the *d*-isomeride.

d-**Galactose** is formed together with *d*-glucose by the hydrolysis of milk-sugar with dilute acid, and also from certain gums. It crystallizes in slender needles, and melts at 166°, is

dextro-rotatory, $[\alpha]_D = +80{\cdot}3°$, and readily fermented. Its **pentacetyl** derivative melts at 143° (for four isomeric forms, cf. *Hudson*, J. A. C. S. 1915, **37**, 1589; 1916, **38**, 1223), α-**methyl-galactoside** at 111°, and the stereo-isomeric β-**compound** at 173°–175°.

Talose is a syrup. The phenyl-hydrazone is very readily soluble in water (difference from galactose).

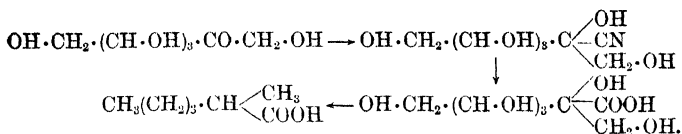
Ketohexoses, $OH{\cdot}CH_2{\cdot}[CH{\cdot}OH]_3{\cdot}CO{\cdot}CH_2{\cdot}OH$, are structurally isomeric with the aldohexoses. As ketones they cannot be oxidized to acids containing the same number of carbon atoms (cf. p. 314). Although ketones, they can reduce alkaline copper solutions. The formula contains 3 asymmetric carbon atoms, and hence numerous stereo-isomerides are theoretically possible.

d-**Fructose**, *Fruit-sugar* or *lævulose*, $C_6H_{12}O_6$, is almost invariably found along with *d*-glucose in the juice of sweet fruits and also, together with the latter, in honey. It is formed along with *d*-glucose by the inversion of cane-sugar, and together with *d*-mannose by the cautious oxidation of *d*-mannitol; also from *d*-phenyl-glucosazone, and therefore indirectly from *d*-glucose. It is most easily prepared by heating inulin (p. 339) with very dilute acid (B. **23**, 2084); is somewhat difficult to obtain crystalline, and then forms hard, anhydrous, rhombic crystals melting at 95°. It is lævo-rotatory, although belonging genetically to the *d*-series, and has $[\alpha]_D^{20} = -92°$. It may be separated from *d*-glucose by means of its sparingly soluble lime compound.

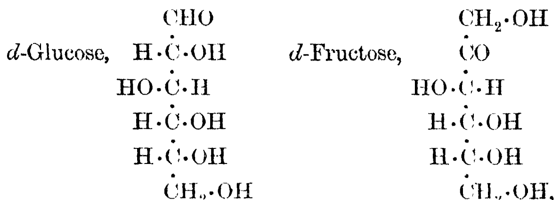
Its close relationship to *d*-glucose is shown by the fact that it yields the same osazone, and on reduction yields a mixture of *d*-mannitol and *d*-sorbitol. On oxidation it yields glycollic and tartaric acids, or glycollic and trihydroxy-butyric acids (cf. p. 314). With methyl-phenyl-hydrazine it yields a colourless **osazone.** It is fermentable, but not so readily as *d*-glucose. It is manufactured from inulin for the use of diabetic patients in the place of cane-sugar.

l-**Fructose** closely resembles *d*-fructose, but is dextro-rotatory, and as it is not readily fermented, can easily be obtained from *i*-**fructose**, which is a syrup.

Constitution of *d*-Fructose.—The general properties point to its ketonic structure, and this was further proved by *Kiliani*, who hydrolysed the cyanhydrin, and then reduced the hydroxy-acid thus obtained with hydriodic acid and phosphorus, and obtained methyl-butyl-acetic acid:



Its configuration as *hexanepentol-2-one* − + + follows from its close relationship to *d*-glucose.



since both yield the same osazone.

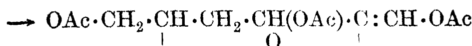
Other stereo-isomeric ketohexoses are *d*-**tagatose**, obtained by the action of potassium hydroxide solution on *d*-galactose. It melts at 124°, and yields the same osazone as *d*-galactose. *d*-**Sorbose**, obtained by oxidizing *d*-sorbitol; and *l*-**sorbose**, obtained as a by-product in the preparation of *d*-tagatose. The fructoses correspond in configuration with the arabinoses, tagatose with lyxose, and the sorboses with the xyloses.

Resolution of Racemic Sugars.—One method is by means of *d*-phenylamyl-hydrazine, $C_6H_5N(C_5H_{11})\cdot NH_2$, separating the two phenylamyl-hydrazones by fractional crystallization and regenerating the active sugars by hydrolysis. (*Neuberg*, B. 1905, **38**, 868). Another method consists in combining the aldose with an active mercaptan, *e.g.* *d*-amylmercaptan. *d*-*l*-Arabinose reacts with *d*-amylmercaptan, giving a mixture of two isomerides, viz. *d*-**arabinose**-*d*-**amylmercaptal** and *l*-**arabinose**-*d*-**amylmercaptal**, $OH\cdot CH_2(CH\cdot OH)_3\cdot CH(SC_5H_{11})_2$, which can be separated by fractional crystallization from alcohol, in which the former is less soluble (Abs. 1916, **i**, 308).

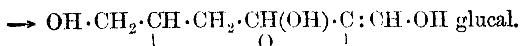
Unsaturated Monosaccharoses.—**Glucal**, $C_6H_{10}O_4$, is a syrup obtained by the following series of reactions:—Acetobromoglucose reduced with zinc and acetic acid gives triacetylglucal, and this when hydrolysed yields glucal. During the reduction of the acetobromoglucose a molecular rearrangement occurs, and the ethereal O atom no longer remains attached to a terminal C atom.



$$OAc\cdot CH_2\cdot CH(OAc)\cdot CH\cdot CH(OAc)\cdot CH(OAc)\cdot CHBr$$ (O bridge)



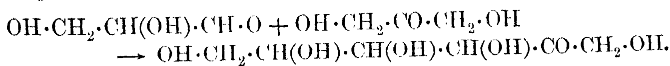
$$\rightarrow OAc\cdot CH_2\cdot CH\cdot CH_2\cdot CH(OAc)\cdot C:CH\cdot OAc$$ (O bridge)



$$\rightarrow OH\cdot CH_2\cdot CH\cdot CH_2\cdot CH(OH)\cdot C:CH\cdot OH \text{ glucal.}$$ (O bridge)

When reduced **dihydroglucal**, $C_6H_{12}O_4$, m.-p. 86°, is obtained, and this does not show unsaturated or reducing properties (*E. Fischer*, B. 1914, **47**, 196). Glucal has been isolated from the hydrolytic products of nucleic acid (Z. physiol. 1917, **100**, 241). For other glucals see B. 1928, 1825.

Synthesis of Hexoses.—Four methods have been used for synthesizing hexoses. 1. The polymerization of formaldehyde by means of lime water (*O. Loew*, 1886). The product was termed **formose**, but has since been shown to be a mixture of hexoses containing **α-acrose**. 2. By the addition of bromine to acrolein and the decomposition of the dibromide with barium hydroxide (*E. Fischer* and *Tafel*). Glyceraldehyde (p. 228) is first formed, and this may then undergo the aldol condensation. 3. By the action of barium hydroxide on glycerose (p. 317), and hence a synthesis from glycerine. Two isomeric hexoses were isolated, viz. α- and β-acroses (*E. Fischer* and *Tafel*, B. 1887, **20**, 1093, 3384; 1889, **22**, 97). The synthesis consists in an aldol condensation of the two components of glycerose, viz. glyceraldehyde and dihydroxy-acetone:



$$OH\cdot CH_2\cdot CH(OH)\cdot CH\cdot O + OH\cdot CH_2\cdot CO\cdot CH_2\cdot OH$$
$$\rightarrow OH\cdot CH_2\cdot CH(OH)\cdot CH(OH)\cdot CH(OH)\cdot CO\cdot CH_2\cdot OH.$$

Pure glyceraldehyde also yields the two hexoses under similar c[illegible]ns, due to the conversion of part of the aldehyde i[illegible]roxyacetone. 4. By the action of alkalis on glycolal[illegible]H·CH_2·CHO (p. 212; *Jackson*, J. C. S. 1900, **77**, 129), [illegible] $C_4H_8O_4$, and α- and β-acroses are formed and [illegible] means of their oxazones. The α-acrose obt[illegible]ions has been the starting-point for the synt[illegible] other hexoses. The α-acrose is converted [illegible] its osazo[illegible] this is hydrolysed to the osone, and then reduced to the [illegible]se, when *d-l*-fructose is obtained. The osazone obtained fr[illegible]α-acrose is identical with *d-l*-glucosazone, but as the same osazone is formed from glucose,

mannose, and fructose, the identity of the original α-acrose is not established. According to *Neuberg* (B. 1902, **35**, 2626) and *Schmitz* (B. 1913, **46**, 2327), α-acrose is in reality *d-l*-fructose, as it has been obtained crystalline, m.-p. 129–130°, and has been found to react with methylphenylhydrazine, which does not form osazones with aldoses. Similarly it has been shown that β-acrose is *d-l*-sorbose. Thus the primary products are both ketoses formed by the condensation of glyceraldehyde with dihydroxyacetone. The scheme (p. 327) gives a *résumé* of the steps involved in the synthesis of the other hexoses from α-acrose. *Stoklasa* (C. R. 1913, **156**, 646) has shown that radium emanation causes hydrogen to reduce carbon dioxide to formaldehyde in the presence of $KHCO_3$, and that the aldehyde then polymerizes to a mixture of reducing sugars.

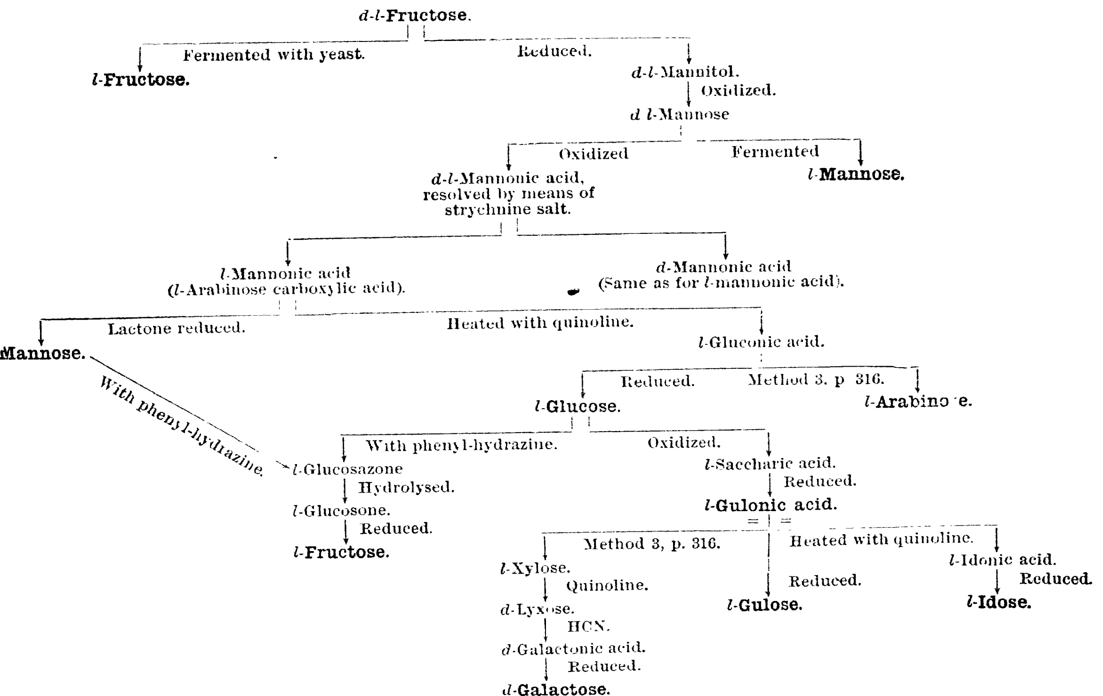
Action of Alkalis on Hexoses.—This action has been studied by *Lobry de Bruyn* (B. **28**, 3078; Rec. 1897, **16**, 274), who has shown that glucose, mannose, and fructose are partially transformed into each other under the influence of dilute alkalis. Fructose is an intermediate product in the conversion of glucose into mannose and an inactive hexose, $C_6H_{12}O_6$, **glutose**, a constituent of sugar-cane molasses, is also formed.

Nef. (A. 1910, **376**, 1; 1914, **403**, 204) has made a more extended investigation of the action of alkalis on hexoses and of the oxidation of the products. In alkaline solution they are extremely readily oxidized even by atmospheric oxygen.

B. Di- and Trisaccharoses

This group comprises those carbohydrates which may be regarded as derived from 2 or 3 molecules of a monose by the elimination of 1 or 2 mols. of water respectively. As such anhydrides, they are all readily hydrolysptaihen boiled with dilute acids, yielding monoses, usually ·CH(SC Thus cane-sugar yields a mixture of *d*-glucose andstallizatiose; maltose yields *d*-glucose only; milk-sugar yi Abs. 19 ucose and *d*-galactose: $C_{12}H_{22}O_{11} + H_2O = 2\,C_6H$, C_6H_{1}

Raffinose or melitriose is a type of actionscharose, and on hydrolysis yields melibiose and *d*-fructcid. The hydrolysis in most of these cases can not only be ef l. ed by means of acids, but also by means of sucroclastic arymes, *e.g.* diastase and invertase hydrolyse cane-sugar, ma ase malt-sugar, &c. The readiness with which the disaccharoses are hydrolysed indicates


d-l-Fructose.
Fermented with yeast.
l-Fructose.
Reduced.
d-l-Mannitol.
Oxidized.
d l-Mannose
Oxidized
Fermented
l-Mannose.
d-l-Mannonic acid,
resolved by means of
strychnine salt.
l-Mannonic acid
(l-Arabinose carboxylic acid).
d-Mannonic acid
(Same as for l-mannonic acid).
Lactone reduced.
Heated with quinoline.
Mannose.
l-Gluconic acid.
With phenyl-hydrazine.
Reduced.
Method 3. p 316.
l-Glucose.
l-Arabinose.
With phenyl-hydrazine.
Oxidized.
l-Glucosazone
Hydrolysed.
l-Glucosone.
Reduced.
l-Fructose.
l-Saccharic acid.
Reduced.
l-Gulonic acid.
Method 3, p. 316.
Heated with quinoline.
l-Xylose.
Quinoline.
d-Lyxose.
HCN.
d-Galactonic acid.
Reduced.
d-Galactose.
Reduced.
l-Gulose.
l-Idonic acid.
Reduced.
l-Idose.

a union of the 2 molecules of monose by means of oxygen and not of carbon. The disaccharoses are thus ethereal anhydrides of the hexoses, *e.g.* cane-sugar is *d*-glucose-*d*-fructose anhydride, and malt-sugar *d*-glucose anhydride, &c. In this anhydride formation 8 of the original 10 OH groups have remained intact, as the disaccharoses readily yield **octamethyl** and **octacetyl** derivatives and **octa-nitrates** (J. A. C. S. 1919, **41**, 235):



$$2\,C_6H_7O(OH)_5 = [C_6H_7O(OH)_4]_2O + H_2O.$$

As a rule, 2 stereo-isomeric octa-acetyl derivatives are obtained from each disaccharose (*Hudson* and *Johnson*, *ibid.* 1915, **37**, 1270, 1276), and these are related in much the same manner as α- or β-methyl glucosides (Chap. XLVII, I.).

As milk-sugar and malt-sugar both reduce *Fehling's* solution, it is highly probable that they still retain a CHO group of one of the component monose molecules. And as cane-sugar is not a reducing sugar, it probably contains no carbonyl group. The chief difficulty in assigning structural formulæ to the disaccharoses is to determine the oxygen atoms which take part in the anhydride formation, and to determine with certainty which of the 4 stereo-isomeric forms of a particular monose (*e.g.* α, β, γ, δ glucose) has taken part in the anhydride formation. For details see Enzymes, Chap. XLVIII, B.

The compounds possess for the most part a sweet taste, and crystallize more readily and are more stable than the monoses, but resemble the latter in solubility. They are not directly fermentable, but can be fermented after hydrolysis to monoses. All those which occur naturally are optically active.

Cane-sugar or **Sucrose**, *Saccharobiose*, $C_{12}H_{22}O_{11}$, occurs in red beet (Beta) 16–20 per cent, in the sugar-cane (Saccharum) 14–26 per cent in the juice, in the sugar-maple (Sorghum), together with invert sugar in the mahua flower (*Bassia latifolia*), and in many other plants, chiefly in the stem.

Preparation.—(*a*) From sugar-cane by expressing the juice and evaporating it until crystallization begins. (*b*) From sugar-beet by a systematic extraction of the pulp with water, *e.g.* by the "diffusion process". The impure juice is then treated with lime ("defecation"), the excess of the latter thrown down by carbon dioxide ("saturation"), and the syrup filtered through animal charcoal, and evaporated *in vacuo* to crystallization. From the mother-liquid of molasses the crystallizable sugar still present can be obtained as the sparingly

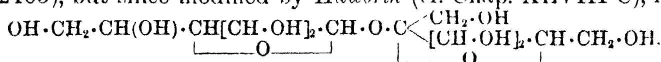
soluble strontium saccharate, $C_{12}H_{22}O_{11}$, SrO, which is then suspended in water and decomposed by carbon dioxide ("desugarizing of molasses").

Cane-sugar crystallizes in large monoclinic prisms, as is well seen in sugar-candy, and is soluble in one-third of its weight of water. It is not turned brown when heated with potash, and yields saccharates with lime and strontia, *e.g.* $C_{12}H_{22}O_{11} + CaO + 2H_2O$; $C_{12}H_{22}O_{11} + 2CaO$; $C_{12}H_{22}O_{11} + 3CaO$. Concentrated sulphuric acid produces charring (difference from *d*-glucose). Cane-sugar melts at 160°, and remains in the amorphous condition for some time after cooling (barley-sugar); when heated more strongly, it becomes brown from the formation of caramel or sugar dye, and finally chars.

The percentage of sugar in a solution of unknown strength can be determined from the specific rotatory power ($[\alpha]_D^{20°} = +66{\cdot}5°$) by measuring the angle (α) through which the plane of polarization is turned when a ray of polarized light is passed through a layer of the solution of known length. This is known as saccharimetry.

It is readily hydrolysed by acids, and this process is commonly spoken of as the **inversion** of cane-sugar, and the product as **invert sugar**. These names are due to the fact that the hydrolysis is accompanied by a change in the optical activity of the solution. The solution of cane-sugar is dextrorotatory, but after hydrolysis (or inversion) it becomes lævorotatory, as *d*-fructose is more strongly lævo- than *d*-glucose is dextro-rotatory.

Sucrose itself does not reduce *Fehling's* solution, but after inversion readily reduces. This would indicate that in the anhydride formation the aldehydic group of *d*-glucose and the ketonic group of *d*-fructose have been destroyed. The constitutional formula suggested by *E. Fischer* (B. 1893, 26, 2405), but since modified by *Haworth* (cf. Chap. XLVIII C), is:



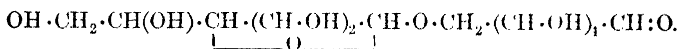
This formula readily accounts (*a*) for the formation of an octacetyl derivative (m.-pt. 67°) and an octamethyl ether; (*b*) for the absence of all reducing properties; (*c*) for the readiness with which it can be hydrolysed, since the two hexose molecules are united by means of an atom of oxygen; (*d*) for the non-formation of a hydrazone.

Milk-sugar or **Lactose**, *Lactobiose*, $C_{12}H_{22}O_{11} + H_2O$, occurs

in milk, and only occasionally in the vegetable kingdom. It is obtained by evaporating sweet whey. It crystallizes in hard rhombic prisms, and is much less sweet than cane-sugar, and also much less soluble in water. It is converted into "lacto-caramel" at 180°. It shows muta-rotation (p. 321), and reduces *Fehling's* solution. The anhydrous sugar occurs in α and β forms.

Maltose or **Malt-sugar,** *Maltobiose,* $C_{12}H_{22}O_{11} + H_2O$, is formed by the action of diastase upon starch during the germination of cereals (preparation of malt). It forms a hard white crystalline mass, very similar to grape-sugar, and strongly dextro-rotatory + 137°. It reduces *Fehling's* solution, but only to about two-thirds the extent to which *d*-glucose does.

Lactose and maltose resemble one another very closely, and are probably stereo-isomeric. Since they both possess reducing properties, yield hydrazones, cyanhydrins, and can be oxidized to monobasic acids containing the same number of carbon atoms, it is obvious that they must contain an aldehydo-group, and the following structural formula was assigned to both by *E. Fischer* (B. 1893, **26**, 2405; see, however, Chap. XLVII, H.):—



$$OH \cdot CH_2 \cdot CH(OH) \cdot \underbrace{CH \cdot (CH \cdot OH)_2 \cdot CH}_{O} \cdot O \cdot CH_2 \cdot (CH \cdot OH)_4 \cdot CH{:}O.$$

Lactose and maltose are not fermentable until after hydrolysis. Certain micro-organisms contain an enzyme **lactase** which hydrolyses the former, and it is then fermented by yeasts. After hydrolysis it can be converted into lactic acid by certain species of bacteria. Maltose is hydrolysed by the enzyme maltase.

In the formation of the lactose molecule it is the CHO group of the galactose which is destroyed, as on oxidation **lactobionic acid,** $C_{12}H_{22}O_{12}$, is formed, and when hydrolysed this yields galactose and gluconic acid.

Revertose is the name given to the disaccharose obtained by *Croft-Hill* (J. C. S. 1903, **83**, 580) by the synthetic action of the enzyme maltase on *d*-glucose. It has $[\alpha]_D = + 91 \cdot 5°$, and yields an osazone melting at 173° (corr.). It may be identical with *Fischer's* isomaltose (*E. F. Armstrong*, P. R. S. 1905, **76** B., 592).

Cellobiose or **Cellose** is a disaccharose, $C_{12}H_{22}O_{11}$, obtained by incomplete hydrolysis of cellulose (p. 333) by means of acetic anhydride and sulphuric acid, in the form of its **octa-**

acetate, m.-p. 228-229°. Yield 50 per cent. The sugar itself obtained by hydrolysing the acetate with alcoholic potash forms a colourless crystalline powder practically insoluble in alcohol or ether. It reduces *Fehling's* solution, exhibits muta-rotation, has $[\alpha]_D = +34 \cdot 6°$, is not fermented by yeast, and on hydrolysis with acids yields *d*-glucose. It is hydrolysed by maltase, and by an enzyme contained in apricot kernels and termed **cellase**. Its **osazone** melts at 208–210°, and bromine water oxidizes the sugar to **cellobionic acid.**

Gentiobiose is a reducing disaccharose obtained by incomplete hydrolysis of the tri-saccharose, gentianose, with 0·2 per cent sulphuric acid or invertase. It melts at 190–195°, has a bitter taste, and shows muta-rotation; the final value is $[\alpha] + 9 \cdot 8°$. It is not fermented by yeast.

Trehalose, $C_{12}H_{22}O_{11}$, $2\,H_2O$, is a non-reducing sugar found in fresh moulds and in manna. It is non-reducing, and has $[\alpha]_D = +197$, and on hydrolysis it yields *d*-glucose.

Isomaltose was obtained synthetically by *E. Fischer* (B. 1895, **28**, 3025) by the condensing action of hydrochloric acid on glucose. It is non-fermentable and yields an **osazone** with m.-p. 150°.

Melibiose, $C_{12}H_{22}O_{11}$, $2\,H_2O$, one of the hydrolytic products of raffinose when dilute acids or top yeasts are used, is a reducing sugar, is less sweet than cane-sugar, exhibits muta-rotation, $[\alpha]_D = +143°$, and on further hydrolysis yields *d*-glucose and *d*-galactose. Its **osazone** melts at 178–179°.

Several disaccharoses derived from *d*-glucose and *d*-galactose have been synthesized from aceto-chloro-glucose + *d*-galactose, and from *d* aceto-chlor-galactose and *d*-glucose (B. 1902, **35**, 3145).

Disaccharoses derived from condensed hexose and pentose molecules are also known (B. 1898, **31**, 537; 1900, **33**, 2091; Bull. Soc. 1911, **9**, 38, 84, 147).

Raffinose or *Melitriose*, $C_{18}H_{32}O_{16} + 5\,H_2O$, is found in the sugar-beet, and therefore in molasses, in the manna of the eucalyptus, and in cotton-seed cake, &c. It is very like cane-sugar but tasteless, is strongly dextro-rotatory, and does not reduce *Fehling's* solution. When inverted, it yields in the first instance *d*-fructose and melibiose, the latter then breaking up into galactose and *d*-glucose. (For its constitution, see B. 1889, **22**, 3118; also A. **232**, 169.)

Gentianose, $C_{18}H_{32}O_{16}$, is present together with cane-sugar in the fresh root on *Gentiana lutea*; it melts at 207–209° (corr.),

has $[\alpha]_D + 31 \cdot 5°$, it does not reduce *Fehling's* solution, and on hydrolysis yields gentiobiose and *d*-fructose.

Stachyose, $C_{24}H_{42}O_{21}, 4\frac{1}{2}H_2O$, which is found in the roots of *Stachys tuberifera* and of several *Labiatiæ*, is an example of a tetra-saccharose. Anhydrous, it melts at 170° and has $[\alpha]_D = +149°$. Invertase, maltase, or acetic acid hydrolyse it, yielding *d*-fructose and **manninotriose**, and on further hydrolysis the latter yields *d*-galactose (2 mols.) and *d*-glucose (1 mol.).

C. Polysaccharoses

The empirical formula of the members of this series is $C_6H_{10}O_5$, but they all possess a much higher molecular weight, *e.g.* $(C_6H_{10}O_5)_n$. They are for the most part amorphous and tasteless, insoluble in alcohol and ether; a few are soluble in cold water, but the majority not; thus cellulose is insoluble and also mucilage, the latter merely swelling up with water, while starch forms a jelly with hot water. When boiled with dilute acids or subjected to the action of enzymes, they are hydrolysed to mono- or disaccharoses, generally to hexoses, *e.g.* $C_6H_{10}O_5 + H_2O = C_6H_{12}O_6$. The formation of pentoses is frequently to be noticed in this decomposition.

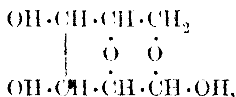
They must therefore be regarded as anhydrides of the monosaccharoses. The hydrolysis proceeds in stages and intermediate products, such as cellose in the case of cellulose and dextrines and maltose in the case of starch, have been isolated.

Although the polysaccharoses are compounds of fundamental importance in the synthetic processes taking place in the living plant tissue, very little is known about their actual constitution. The majority only form colloidal solutions, and the determination of accurate molecular weights is not possible. They still contain free hydroxyl groups as they form esters with nitric and acetic acids, and ethers with methyl sulphate. The monosaccharose units which take part in the formation of these complex carbohydrates are:—*d*-glucose, *d*-fructose, *d*-mannose, *d*-galactose, *l*-arabinose, *l*-xylose, and fucose. The investigations on the polysaccharoses have, to a large extent, been limited to studies of their hydrolyses, and, as they are so widely distributed in the vegetable kingdom, to the discovery of new commercial methods of utilizing them.

Cellulose

This name has been given to a variety of different products from the vegetable kingdom. There are the celluloses proper, the compound celluloses, and the hemicelluloses.

The cellulose proper is met with in cotton-wool, linen, and Swedish filter-paper, and is best obtained by extracting filter-paper or cotton-wool successively with caustic potash, hydrochloric acid, water, alcohol, and ether. When air-dried it forms a white amorphous powder containing 6–8 per cent of moisture, which can be removed by gently warming under reduced pressure. At 150° cellulose begins to decompose, and when subjected to destructive distillation gives combustible gases, acetic acid, acetone, phenol, furfuraldehyde, and other products. When cellulose or starch is distilled under reduced pressure at 200–300°, appreciable amounts of *l*-**glucosan,**



are formed: this can also be obtained from the glucosides of *Coniferæ*, and cellulose is probably a condensation product derived from this (*Pictet* and *Saradin*, C. R. 1918, **166**, 38). It is insoluble in the ordinary reagents, but dissolves in an ammoniacal solution of cupric oxide (*Schweitzer's* Reagent), and is reprecipitated on the addition of acids, alkalis, or salts. It also dissolves in a concentrated solution of zinc chloride. With iodine it gives a yellow or brown coloration, but in the presence of concentrated sulphuric acid a blue colour is developed. A simple glucose anhydride, $C_6H_{10}O_5$, **cellosan,** which is soluble in water is formed when cellulose triacetate is heated with naphthalene at 235° and acetyl groups subsequently removed. From lichnin acetate an isomeric **lichnosan** is formed.

Parchment-paper is unglazed paper which has been immersed for a very short time in concentrated sulphuric acid and then thoroughly washed; the acid transforms a superficial layer of the cellulose into **amyloid.** Cellulose also gives a blue colour with a solution of iodine in zinc chloride and potassium iodide solution. It is usually estimated by *Cross* and *Bevan's* method, which consists in converting all other

materials into soluble products by means of moist chlorine, then washing thoroughly and weighing the dried cellulose. (For discussion on cellulose, cf. *Cross* and *Bevan*, J. S. Dyers, 1918, **34**, 91; J. Soc. Arts, 1920.)

The following are the more important cellulose derivatives, many of which are of considerable commercial value:—

Cellulose hydrates. These are products which closely resemble cellulose in composition, do not possess reducing properties, but are extremely hygroscopic. An important representative of this class is **mercerized cotton**, obtained by the action of cold, concentrated (15–25 per cent) sodium hydroxide on cotton. It is characterized by the readiness with which it can be dyed. **Hydrocelluloses**, obtained by the action of cold, concentrated acids, or by boiling with acetic acid containing two per cent of sulphuric acid, still retain their fibrous structure but are readily ground to a powder; they are less hygroscopic than cellulose and have pronounced reducing properties. **Oxycelluloses** are products formed by the action of oxydizing agents on cellulose. They dissolve in dilute sodium hydroxide solution, yielding golden-yellow solutions, have strong reducing properties, and appear to contain reactive carbonyl groups, and react with phenyl hydrazine. They give a red coloration with aniline, and are less stable and more reactive than the celluloses proper. When boiled with hydrochloric acid they yield furfuraldehyde, which can be estimated by means of phloroglucinol. This reaction is used not merely for detecting but for estimating oxycelluloses. The oxycelluloses are widely distributed in nature, usually in the form of compound celluloses. Thus they are present in the celluloses from woods and lignified tissues generally, and are the chief constituents of the celluloses from cereal, straws, and esparto. According to *Heuser* and *Haug* (Z. Angew. 1918, **31**, 99, 103, 172), straw cellulose is a mixture of normal cellulose and pentosans, and is not a natural oxycellulose. It is highly probable that the substances termed cellulose hydrates, hydrocelluloses, and oxycelluloses are not chemical entities but mixtures of different products.

Cellulose gives rise to a **peroxide** when treated with bleaching powder, acidified ammonium, persulphate, ozone, or other oxidizing agents. This is destroyed by treatment with sodium thiosulphate.

Cellulose can undergo fermentation by means of certain

species of bacteria. Certain species tend to form methane and others hydrogen, but in both cases carbon dioxides and fatty acids (acetic and butyric) are also formed. (*Omelianski*, Abs. 1902, ii, 468; 1906, ii, 278; *Pringsheim*, *ibid.* 1913, i, 1281.)

Cellulose Esters

The cellulose esters are compounds of considerable commercial importance. The acetates, especially those containing five acetyl groups for each C_{12} cellulose unit and soluble in acetone, are largely used for dopes for aeroplane wings, also for making collodion, photographic films, celluloids, and other purposes. (*E. C. Worden*, J. Ind. 1919, **38**, 370, T.) For the manufacture of these products mill waste is generally used.

The nitric esters, so called nitro-celluloses, are used for a variety of purposes, and are usually prepared by the action of a mixture of nitric and sulphuric acids on the carbohydrate. The nature of the product depends largely on the concentration of the acid mixture and upon the temperature. In order to render the products stable, it is necessary to remove all traces of free acid. **Collodion**, a tetranitrate, is soluble in a mixture of alcohol and ether (1 : 7), and the solution is largely used for coating materials and rendering them air-tight. It is also used for the manufacture of artificial silk and in photography. When mixed with camphor (various other substitutes, such as phenolic esters, are now used) it forms ordinary celluloid.

Pyroxylin, 11·2 to 12·4 per cent of nitrogen, is more soluble in many organic solvents than gun-cotton, and is the basis of most "cellulose" lacquers, paints, and enamels. It is usually mixed with gums or resins, and when the solvent is removed a film of excellent finish and hardness and of rapid drying power is obtained (J. Ind. 1927, 336).

The solvents commonly employed are ethyl, butyl and amyl acetates, acetone, methyl-ethyl ketone and ethyl lactate, and these are usually mixed with benzol, or more commonly petroleum spirit.

Gun-cotton, 12·4 to 13 per cent nitrogen, is probably a hexanitrate; in appearance it resembles cotton-wool, but is not so soft. It burns readily and explodes when struck or strongly heated. It is largely used for making smokeless powders, cordite, blasting gelatines, &c., and is often met with in the form of compressed cakes.

Practically all artificial silks, **Rayon**, are cellulose derivatives. The oldest method (*Chardonnel*) consisted in dissolving cellulose nitrates in a mixture of alcohol and ether (3:2), and forcing the solution under pressure from a copper vessel through small capillary tubes into water. The thread thus obtained was stretched to about the thickness of natural silk, and as it became hard was wound, dried, and denitrated by treatment with a reducing agent, such as ammonium sulphide or cuprous chloride and hydrochloric acid.

Other methods which are now adopted consist in (*a*) the use of cellulose acetates obtained by the action of acetyl chloride and zinc acetate or quinoline, or of acetic anhydride and a mineral acid on cellulose. The solution of the acetate is squirted into alcohol through small holes. (*b*) The use of a solution of cellulose in ammoniacal cupric oxide, and forcing the solution through small holes into dilute acid (*Pauly*). (*c*) Use of viscose.

Artificial human and horse hair are manufactured by similar methods. The artificial silks are used for the manufacture of fabrics, and also for insulating metallic wires. (Cf. *Wilson*, J. Ind. 1917, **36**, 817). **Viscose** (*Cross* and *Bevan*) is the sodium salt of cellulose xanthate. Cotton fibre is allowed to swell by treatment with sodium hydroxide solution, and is then shaken with carbon disulphide. Its solution in water forms a gelatinous mass which can be moulded. When exposed to the air it shrinks and hardens to a horn-like mass. It is used as a substitute for glue, celluloid, horn, ivory, &c. When used for the manufacture of artificial silk it is necessary to purify it; this is done by acidifying with a weak acid (acetic or lactic), precipitating with alcohol or brine, and washing.

Viscoid is a mixture of viscose with clay or zinc oxide, and sets to an extremely hard mass.

Compound Celluloses

These comprise the natural products in which the cellulose molecules are united to those of a different type and include ligno-celluloses, pecto-celluloses, muco-celluloses, adipo-celluloses, and cuto-celluloses.

The **ligno-celluloses** are compounds of lignin or lignone, $C_{19}H_{22}O_9$, and cellulose, and are met with in jute and in most woods or lignified tissues of perennial stems. It is probable

that the non-cellulose portion of the molecule consists of a cyclo-hexenedione.

In the pecto- and muco-celluloses the non-cellulose constituents are colloidal forms of carbohydrates or allied derivatives, hemi-celluloses, which are easily hydrolysed to pectin or pectic acids, and these readily gelatinize. The main flax fibre consists of pecto-celluloses, as does China grass or rhamie. In the adipo- and cuto-celluloses the cellulose is associated with fatty and waxy compounds of high molecular weight. The best-known representative is cork in which the cellulose is combined or mixed with cutin and suberin which appear to be glycerides of complex acids such as stearo-cutic. (For rafia, see *Cross* and *Bevan*, J. S. Dyers, 1919, **35**, 70.)

The celluloses in the more or less raw state form the staple of the linen and cotton industries; in the paper industry they are subjected to preliminary treatment, and in the form of derivatives they are the bases of the artificial-silk industry.

Paper. The old method of manufacturing paper was to treat flax or cotton to processes of hydrolysis, *e.g.* treatment with dilute caustic soda, under pressure, and then bleaching, either sun bleaching or, subsequently, bleaching with chlorine or bleaching powder. Such paper is termed rag paper and, on the whole, is very resistent, and can be preserved for centuries without deterioration.

The object of the treatment with alkali and also of the bleaching agent is to remove by hydrolysis or oxidation the non-cellulose constituents in the original fibre, as these are much more readily attacked than the cellulose proper.

With the increase in the demand for cheap paper other raw materials, *e.g.* esparto grass, straw, bamboo and wood-pulp have been introduced, and the result has been a considerable deterioration in the quality of paper and in its keeping properties. This is explicable when it is remembered that esparto cellulose is largely an oxycellulose which is far less resistent to chemical action than a true cellulose, and that mechanical wood-pulp contains all the lignin of the original wood.

Chemical wood-pulp is now usually made by digesting the disintegrated wood with calcium bisulphite under pressure. The bisulphite produces a disintegration of the lignin; after removal from the autoclaves the pulp is washed, bleached, and again washed, and is then ready for conversion into paper. As a rule, sizing materials, *e.g.* rosin and alum, are mixed with

the pulp, and a final sizing with gelatine is applied in order to make the surface less porous.

By-products are now obtained from the waste sulphite liquors. These can be evaporated and the residue subjected to destructive distillation for the production of acetone, methyl alcohol, &c., or they can be fermented by a special species of yeast and ethyl alcohol isolated (1 per cent of volume of liquor). (Cf. *Johnsen*, J. Ind., 1918, **37**, 129, T.)

Sodium sulphate mixed with sodium sulphide is also used for treating wood-pulp under pressure, and the product known as "sulphate pulp" is largely used in Scandinavia for manufacturing stout packing papers known as "Kraft paper".

The **hemi-celluloses** or reserve celluloses are anhydrides of monosaccharoses; they are not soluble in water but are readily hydrolysed by dilute mineral acids, to soluble monosaccharoses, and in this respect differ from the celluloses proper. These products are usually mixtures containing *d*-mannose, *d*-galactose, *l*-arabinose, *l*-xyloxe, and occasionally *d*-fructose and *d*-glucose.

They are present in cells, walls, and in seeds, especially in the husks of shells, *e.g.* peas, vetches, coffee beans, date stones.

Their main function is to serve as reserve cellulose, and during germination of the seed they are used up. Examples of hemi-celluloses are mannane, paramannane, galactane, &c.

Starch or **Amylum**. This is present in the leaves of all assimilating plants, and is formed from carbon dioxide and water in sunlight under the influence of chlorophyll present in the chloroplasts of the cell. It appears to be the final stage of synthesis, soluble sugars are first formed, most of these are transferred by the cell sap to the different parts of the plant for building up plant tissues and only the excess sugar is transformed into starch (*Brown* and *Morris*, J. C. S. 1893, 633), which is never present in large quantities in the leaves. In the absence of sunlight the starch in the leaves is hydrolysed to sugars (maltose) by the aid of the enzyme diastase, and passes into the sap, and is hence known as transitory starch. The great bulk of the starch is always found in the food reservoirs of the plant, *e.g.* rhizomes, tubers, and seeds, it is known as reserve starch, and it is from such sources that starch is always manufactured commercially. The starch in these reservoirs is built up from soluble sugars, probably sucrose (*Brown* and *Morris*), in the absence of carbon dioxide and sunlight by means of the leucoplasts of the cell, and numerous authorities have shown that some of the lower forms of plant

life which are devoid of chlorophyll, *e.g. Spirogyra maxima*, *Bacillus coli*, can synthesise starch from such materials as sucrose, dextrose and glycerol, and in the absence of carbon dioxide certain forms of Algae can make use of formaldehyde-bisulphite for synthesing sugar.

It forms a white, velvety hygroscopic powder, consisting of round or elongated granules built up of concentric layers around a nucleus or hilum, and the form and size of the granules vary considerably with starches from different sources The granules of canna, potato, banana and sago starch are the largest, usually about 60μ, those from lentil, acorn, maize, and wheat are intermediate, and those from certain millets, oat and rice are the smallest (about 15μ).* In wheat starch the granules are nearly spherical and the hilum in the centre, those of the potato are egg or oyster shaped, with an eccentric hilum at the small end of the granule and those from rice and maize are polygonal.

Potatoes contain 15–20 per cent of starch, wheat 60–65, maize 65, and rice 75–80. Arrowroot is obtained from the rhizomes of species of Maranta of the West Indies, and also from the root-stocks of *Curcuma angustifolia* in the East Indies. Sago is derived from the pith of the sago palm (*Sagus lævis*), and tapioca is prepared from the tubers of the cassava (*Manihot utillisima*) of the tropics.

Both the granules of starch and its jelly are coloured an intense blue by iodine and bright yellow by bromine. The colour of the iodide of starch vanishes on heating, but reappears on cooling. The coloration is used as a delicate test for traces of iodine or of starch. Ordinary air-dried starch contains some 10–20 per cent of water, some of which can be removed by heating to 105°.

Starch is insoluble in cold water, but when heated with water the granules swell and burst, forming a viscid opalescent liquid, **starch paste**, which sets to a stiff paste when cold. The temperature at which the change occurs is known as the temperature of gelatinasition and varies from 55–85°, and if the paste is allowed to stand for several days under aseptic conditions it gradually becomes more opaque and yields a deposit of amyloses. This is termed *reversion* and can be accelerated by acids or more particularly by the enzyme *amylocoagulase*.

Very little of a definite nature is known about the structure

* For photo-micro-graphs, see p. 92, Enyon and Lane's *Starch* (Heffer), 1928.

of starch although much work has been done on the subject. It is a carbohydrate complex and undergoes processes of hydrolysis when, (*a*) boiled with dilute sulphuric acid; (*b*) heated to a moderate temperature; (*c*) subjected to the action of a malted grain, *e.g.* barley, *i.e.* to the action of the enzyme diastase. *C. O'Sullivan* (J. C. S. 1872, 579; 1876, 125), showed that the products of diastic fermentation are maltose and dextrin, and that the proportion of maltose in the product decreases as the temperature of conversion is raised above 63°. According to *Brown*, *Heron*, and *Morris* (1879, 596), malt extract at room-temperature converts starch paste into 80·9 parts of maltose and 19·1 parts of dextrin, and the same change occurs at all temperatures to 60°. The intermediate dextrins were investigated by *Brown* and *Morris* (1885, 527; 1889, 449, 462), and by *Brown* and *Millar* (1899, 286). Various views have been held as to the nature of the intermediate products and even of the final products. *Lintner* and *Dull's* view (B. 1893, 2533), that *Fischer's* iso-maltose (p. 331), is one of the final products is incorrect, the product being an impure maltose (cf. however, *Syniewski*, A, 1902, **324**, 212).

Maquenne and *Roux* (C. R., 1905, **140**, 1303), claim that starch is a mixture of two substances *amylose* and *amylopectin*, the former in the interior portion of the granule and the latter in the envelope. The amylose, obtained by reversion, or by heating starch with water under pressure and cooling, gives no coloration with iodine in the solid state, is not readily attacked by diastase, and is scarcely soluble in water at 120°; if, however, it is heated with water under pressure at 150° it dissolves fairly readily; the solution can be filtered, gives a blue coloration with iodine and is completely converted into maltose by malt extract at 56°. It is probable that the amylose and amylopectin are not homogeneous (1908, **146**, 542). *Schryver* and *Thomas* (Bio. J., 1923, **17**, 497), have found that certain starches contain small amounts of hemicelluloses, and according to *Ling* and *Nanji* (J. C. S., 1923, **123**, 2666), the ratio of amylose to amylopectin is constant and equal to 2:1, although their absolute percentages may vary according to the proportion of hemicellulose in the starch. Crystalline dextrins can be obtained by the action of *Bacterium macerans* on starch paste at 45° in the presence of mineral nutrient salts, (*Shardinger*, 1908–11), and these products have been examined by *Pringsheim*, *Langhans*, and *Eissler* (B. 1912, 2533; 1913, 2959), who term them di-, tri-, tetra- and hexa-hexosans accord-

ing to the number of $C_6H_{10}O_5$ groups present.* They belong to two distinct series the α and β, the former being mainly derived from the amylose or internal portion of the starch granules and the latter from the amylopectin. The α-compounds are polymers of a dihexosan $(C_6H_{10}O_5)_2$, (B. 1922, 1446; 1924, 884), and the β-compounds of a trihexosan, $(C_6H_{10}O_5)_3$, both of which have been isolated. Neither hexosan possesses reducing properties, but on treatment with cold concentrated hydrochloric acid they are hydrolysed, the α-compound yields a reducing disaccharose, $C_{12}H_{22}O_{11}$, termed *amylobiose*, and the β-compound or amylopectin a reducing trisaccharose, $C_{18}H_{32}O_{16}$, *amylotriose*, and all the compounds can be quantitatively hydrolysed to maltose by invertases. Structural formulæ have been suggested for the polyhexanoses and the resulting bi- and trisaccharoses. It is thus probable that starch is built up of maltose units and that dihexosan (from amylose) is a maltose anhydride.

Starch, like cellulose, yields *l*-glucosan (45 per cent), (p. 333), when heated under a pressure of 12–16 mm. This is probably an inner anhydride of β-glucose (Chap. XLVII. Muta-rotation) and can be readily polymerised, yielding products analogous to the polyhexosans from starch. For further polyhexosans from starch see *Pictet* and others (Helv., 1924, 932; 1925, 946; 1926, 33), *Ling* and *Nanji* (J. C. S. 1923, 2666; 1925, 629), have studied the enzymatic hydrolysis of starch and its constituents under varying conditions, and they regard amylose as having an α-hexahexosan as basal unit and amylopectin an $\alpha\beta$-hexahexosan as basal unit. For the results of methylation of starch see *Irvine* and *Macdonald* (J. C. S. 1923, 898; 1924, 942; 1926, 1502). According to *Samec* and *Von Hoefft* (Koll. 1912, 132; 1913, 141; 1914, 23, 291), amylopectin owes its characteristics to the presence of a phosphoric acid complex. The amylopectin is a calcium salt and the first action of acid is to liberate the free complex acid which then undergoes hydrolysis, liberating phosphoric acid. The amount of phosphorus present is so small that if the phosphoric acid forms an integral part of amylopectin molecule the latter must be at least 70,000.

Uses of Starch. Wheat starch was used in the middle ages in the laundry and for stiffening fabrics, and in the 18th century for powdering the hair, and in this century potato-starch was introduced. In the 19th century the industry

* The products are sometimes termed di-, tri-, &c., amyloses, but in order to avoid confusion the name amylose is retained for the original constituent of starch, and the degradation products are termed hexosans.

developed in an amazing manner, and both maize and rice were utilised as sources. Starch is used in the sizing of paper, as an adhesive in the manufacture of paste-boards, and in very large quantities in making sizes for treating cotton yarn before it is woven into cloth, the objects being to bind loose threads, to strengthen the yarn, and to hold weighting materials such as china clay. The amount of size incorporated in the yarn varies enormously in different grades, and the starch mainly used is wheat and then potato. Starch, soluble starch and dextrin are also largely used for finishing the woven cotton fabric. Starch and dextrin are used as thickeners in colour printing on cotton as they serve to increase the viscosity of the dye solution. Very large quantities are used for dressing and finishing fabrics after laundering. It is also used as a constituent in custard powders, ice-cream powders and toilet powders, and is the source from which large amounts of glucose and dextrin are manufactured (for manufacture of starch and starch products, soluble starch, dextrins and glucose (cf. *Eynon* and *Lane*, Chaps. VI.–XI.).

Soluble starch is formed (*a*) by leaving starch in contact with cold mineral acids, (*b*) by heating starch with glycerol, (*c*) by boiling starch with water containing a little sulphuric acid, (*d*) by the action of diastase on starch. Prolonged treatment with mineral acids converts starch into dextrins and maltose and finally into *d*-glucose (*Daish*, J. C. S. 1914, **105**, 2053, 2065; for detailed study of action of acids see *Nanji* and *Beazley*, J. Ind., 1926, 215 T.). Ordinary diastase or amylase, a β-diastase, converts starch finally into dextrins and maltose, whereas takadiastase, which contains the enzyme maltase in addition to an α-diastase, yields *d*-glucose as final product. (*Davis* and *Daish*, Abs. 1914, ii, 588. Cf. *Baker* and *Hulton*, J. C. S. 1914, **105**, 1529; *W. A. Davis*, J. S Dyers, 1914, **30**, 249). Saliva and pancreatic juice also hydrolyse starch.

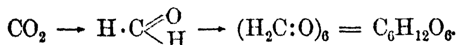
Lichenin or *Moss starch*, present in many lichens, *e.g.* in Iceland moss (*Cetraria islandica*), is coloured a dirty blue by iodine; and **inulin**, present in the tubers of the dahlia and in the roots of chicory (*Inula Helenium*), is coloured yellow by iodine and converted into *d*-fructose when boiled with water.

Glycogen, or **Animal starch**, *Liver starch*, is present, *e.g.* in the livers of the mammalia. It is a colourless amorphous powder which is turned wine-red by iodine; after the death of the animal it rapidly changes into *d*-glucose, the same conversion being effected by boiling with dilute acids, while

enzymes transform it into maltose. For preparation from yeast, see *Harden* and *Young*, J. C. S. 1912, **101**, 1928.

Dextrine, or *Starch gum*, is a comprehensive name applied to intermediate products obtained in the transformation of starch into maltose and *d*-glucose. It may be prepared (*a*) by heating starch either alone or with a little nitric acid, or, even better, in a vacuum at 120° over P_4O_{10}; (*b*) together with *d*-glucose by boiling starch with dilute sulphuric acid; and (*c*) together with maltose by the action of diastase on starch. The dextrines are soluble in water, and are precipitated by alcohol. They are often named according to their reaction with iodine, *e.g.* **amylo-dextrine** blue, **erythro-dextrine** red, and **achroo-dextrine** no colour. They do not reduce *Fehling's* solution even when warmed, and are not directly fermentable by yeast but only after the prolonged action of diastase, glucose being formed as an intermediate product.

Synthesis of Carbohydrates.—The sugars are extremely important from the point of view of plant physiology. The plant absorbs carbon dioxide and water, and with the aid of sunlight is capable, in the presence of chlorophyll, of transforming these into glucose and even more complex carbohydrates, such as starch, and oxygen, equal in volume to the carbon dioxide used, is evolved. Various speculations have been made with regard to the manner in which these complex compounds are formed. *Baeyer* has suggested that the carbon dioxide is first reduced to formaldehyde, and this then polymerizes as in *Loew's* experiments, yielding carbohydrates,



$$CO_2 \rightarrow H\cdot C\langle{}^{O}_{H} \rightarrow (H_2C:O)_6 = C_6H_{12}O_6.$$

For many years the important link in this chain, viz. the reduction of carbon dioxide to formaldehyde, was missing; the reaction could not be accomplished in the laboratory. *Fenton* has shown (J. C. S. 1907, **91**, 687) that when carbon dioxide is passed into water in which sticks of magnesium are immersed, a small amount of the gas is reduced to formaldehyde, especially in the presence of ammonia or phenylhydrazine. *Löb* has also found that moist carbon dioxide yields formaldehyde under the influence of the silent electric discharge (Zeit. Elec. 1905, **11**, 745; 1906, **12**, 282).

More recently *Moore* and *Webster* (P. R. S., 1914 B, 163, 556; 1918 B, 168) have proved that this reduction takes place in ultra-violet light (from quartz lamp) and *Baly*, *Heilbron* and

Barker, who have made a more detailed study of this reaction (J. C. S., 1921, 1025) draw the following conclusions: (1) An aqueous solution of carbon dioxide gives formaldehyde when exposed to light of very short wave-length, and this aldehyde is polymerised to reducing sugars in light of slightly longer wave-length; (2) In the presence of sodium phenoxide or metallic salts such as ferric chloride or uranyl nitrate the aldehyde is formed but does not undergo polymerisation; (3) The photosynthesis of formaldehyde can be photocatalysed by certain basic coloured substances, *e.g.* colloidal uranium and ferric hydroxides malachite-green or methylorange, and the synthesis then takes place in visible light. The polymerisation can be photocatalysed in a similar manner; (4) Carbohydrates, glycerol, acetone, &c., when exposed in aqueous solution to ultra-violet light yield formaldehyde and reducing sugar, and an equilibrium is established between sugar, formaldehyde and carbon dioxide. Chlorophyll appears to be an ideal photocatalyst for both stages of carbohydrate synthesis from carbon dioxide and water.

Grafe (B. Bot. Ges. 1911, **29**, 19) has shown that green seedlings can grow in an atmosphere containing 1·3 per cent of formaldehyde in the absence of carbon dioxide, and numerous authorities have proved the presence of small amounts of formaldehyde in assimilating leaves. Compare *Usher* and *Priestly* (P. R. S. 1906, **77** B 369; **78** B. 318; 1911, **84** B. 101), who show that the normal products of photolysis of carbon dioxide are H_2O_2 and formaldehyde, although under certain conditions formic acid can be produced.

Class II.—CHEMISTRY OF THE CYCLIC COMPOUNDS

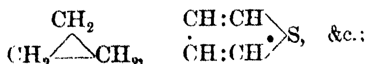
XV. INTRODUCTION

The compounds which have been dealt with in Chapters I to XIV are derivable from the homologous hydrocarbons C_nH_{2n+2}, C_nH_{2n}, C_nH_{2n-2}, &c., by the exchange of hydrogen for halogen, hydroxyl or oxygen, amidogen, carboxyl, &c.; and since all the hydrocarbons already mentioned may also be regarded as derivatives of methane (*e.g.* $C_2H_6 = CH_3(CH_3)$ = methyl-methane, $C_3H_8 = CH_2(CH_3)_2$ = dimethyl-methane, $C_2H_4 = CH_2{:}CH_2$ = methylene-methane, $C_2H_2 = CH{\vdots}CH$ = methine-methane, &c.), we may term the compounds which have been described in the foregoing portion of this book **methane derivatives.**

As nearly all these compounds have open-chain formulæ, they are spoken of as **open-chain compounds**, or often **aliphatic compounds.**

But in addition to this first class of organic compounds there is a second great class, viz. that of the **closed-chain compounds.** The old classification was into aliphatic or methane derivatives and aromatic or benzene derivatives. The expression "aromatic" is historical, but no longer justified by facts, since compounds of agreeable as well as unpleasant odour are to be found in both classes. The members of this second class which are derivable from the hydrocarbon benzene, C_6H_6 (and also from more complicated hydrocarbons such as anthracene, naphthalene, &c., which are themselves derivatives of benzene), just as the methane derivatives are from methane, are designated benzene derivatives.

Recent investigations have led to the discovery of numerous other cyclic compounds which cannot be regarded as simple derivatives of benzene, *e.g.*:



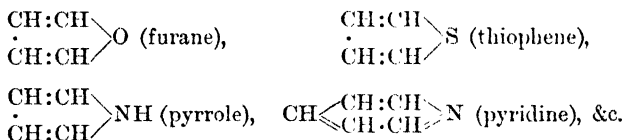
and hence the modern classification of the cyclic compounds is into:—

A. **Carbocyclic or Isocyclic.**—In all these compounds the ring or closed chain is composed entirely of carbon atoms. The carbocyclic compounds are usually divided into—

(i) Polymethylene derivatives or naphthenes.

(ii) Benzene derivatives or aromatic compounds, including the allied compounds naphthalene, anthracene, &c.

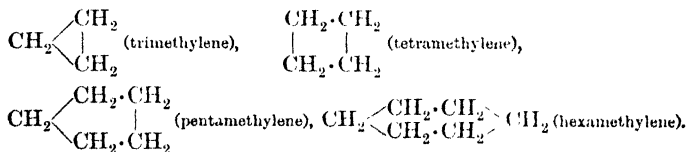
B. **Heterocyclic Compounds.**—In these compounds the closed ring is formed partly of carbon atoms and partly of atoms of other elements. Well-known examples are:



CARBOCYCLIC COMPOUNDS

XVI. POLYMETHYLENE DERIVATIVES

For summary of early work see *Perkin*, J. C. S. 1929, 1347. The hydrocarbons consist of three or more methylene groups united together to form closed rings. The specific names indicate the number of such groups, *e.g.*:



The systematic names for these compounds are **cyclo-propane, cyclo-butane**, &c., although the compounds are isomeric with the olefines, and have the same general formula, C_nH_{2n}. The above names indicate the fact that the compounds are in a sense saturated. The systematic nomenclature for derivatives is similar to that used in the aliphatic series. Thus, $CH\langle^{CH \cdot CH_2}_{CH_2 \cdot CH_2}\rangle$ is termed cyclo-pentene, $CO\langle^{CH_2 \cdot CH_2}_{CH_2 \cdot CH_2}\rangle$ is

cyclo-pentanone, $CH \langle {CH \cdot CH_2 \atop CH_2 \cdot CO} \rangle$ is cyclo-Δ^1-pentene-4-one, and $CO_2H \cdot CH \langle {CH:CH \atop CH_2 \cdot CO} \rangle CH_2$ is cyclo-Δ^2-hexene-4-one-1-acid.

Relative Stability of Polymethylene Compounds. — The majority of trimethylene derivatives are relatively unstable; to a certain extent they resemble ethylene oxide, and are capable of forming additive products by the rupture of the ring, *e.g.* bromine slowly transforms trimethylene under the influence of sunlight into trimethylene dibromide, $Br \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot Br$.

In certain reactions where only cyclo-propane derivatives might be expected, a mixture of both cyclo-propane and -butane compounds is formed (J. C. S. 1899, 48; 1901, 729, 1921, 1582; 1925, 387).

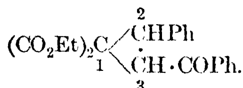
Tetramethylene derivatives are somewhat more stable, and penta- and hexa-methylene derivatives are quite stable and show little or no tendency towards the rupture of the molecule.

Reduction by *Sabatier* and *Senderens'* method (Chap. XLIV, C.), using hydrogen in presence of finely divided nickel, converts trimethylene into propane and tetramethylene into butane (*Willstätter* and *Bruce*, B. 1907, 3979, 4456). When, however, the 7 and 8 C-ring systems are reduced ring degradation occurs (Chap. LII), thus cyclo-heptane yields a mixture of methyl-cyclo-hexane and dimethyl-cyclo-pentane, and cyclo-octane yields dimethyl-cyclo-hexane (B. 1908, 1480). These facts are in harmony with *Baeyer's* tension theory. If the four valencies of the tetravalent carbon atom are assumed to be symmetrically distributed in space around the carbon atom, it is found that ring formation in the case of a cyclo-propane derivative can only take place by the exercise of a considerable strain in the molecule; hence when the ring formation is completed there is considerable tendency for it to spring apart or rupture at some point. With penta- and hexa-methylene compounds, on the other hand, it can be seen by the aid of models that practically no strain is required to complete the ring formation, and thus the rings when once formed are relatively stable. For larger rings, *e.g.* Suberone with C_7 and rings containing 20 or more C atoms see Helv. 1928, 670, 686, also *Vogel*, J. C. S. 1929, 721.

The number of carbon atoms constituting the ring is not the only factor which determines the ease of formation of a ring system or its relative stability when once formed. Rings containing a quaternary carbon atom are difficult to form, and when once formed are relatively unstable, a phenomenon well

illustrated by a comparison of ethyl cyclo-propane-1:1-dicarboxylate and the isomeric 1:2-dicarboxylate (*Goldsworthy* and *Perkin*, J. C. S. 1914, **105**, 2665; *Kenner*, *ibid.* 2685).

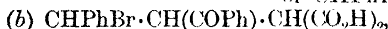
A good illustration of the different ways in which a complex cyclo-propane derivative can undergo fission is met with in ethyl 2-phenyl-3-benzoyl-1:1-dicarboxylate:



Nascent hydrogen opens the ring between C atoms 1 and **3**, yielding products of the type $(CO_2Et)_2CH\cdot CHPh\cdot CH_2\cdot COPh$; alkyl oxides, ammonia and amines produce a fission between atoms 1 and 2, so that compounds of the type $(CO_2Et)_2CH\cdot C(COPh){:}CHPh$ are formed, and lastly, halogen hydrides dissolved in glacial acetic acid attack the union between atoms 2 and 3, and also that between 1 and 2, yielding respectively (*a*) and (*b*) (*Kohler*, J. A. C. S. 1917, **39**, 1404, 1699, 2405):


(*a*) $CHPhBr\cdot C(CO_2H)_2\cdot CH_2\cdot COPh$

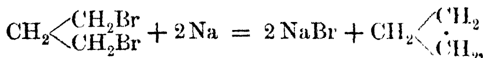

or $CHPhBr\cdot C(CO_2H)_2\cdot CH{:}CPh\cdot OH$,

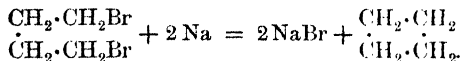

(*b*) $CHPhBr\cdot CH(COPh)\cdot CH(CO_2H)_2$,

and these by the loss of CO_2 and HBr yield respectively the lactone, $CHPh{:}C\langle {CH{:}CPh \atop CO\cdot O}$, and the unsaturated acid, $CHPh{:}C(COPh)\cdot CH_2\cdot CO_2H$.

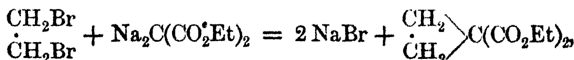
GENERAL METHODS OF FORMATION

1. By the action of sodium on dihalogen derivatives of the paraffins (*Freund*). The two halogen atoms must not be attached to the same or to adjacent carbon atoms.



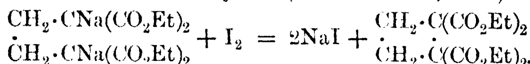


2. Acids and their esters can be obtained by the condensation of ethyl sodio-malonate with ethylene dibromide and other dihalogen derivatives (*W. H. Perkin, Jun.*):



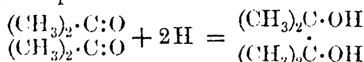
and the ester on hydrolysis yields trimethylene-dicarboxylic acid. Ethyl acetoacetate may be substituted for the malonate.

3. By the action of halogens (bromine, or preferably iodine) on the sodio-derivatives of certain esters, *e.g.* sodio-derivative of ethyl butane-tetracarboxylate (*W. H. Perkin, Jun.*):



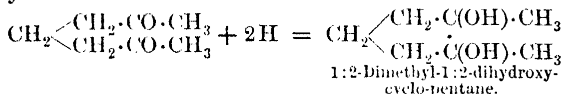
$$\begin{matrix} CH_2\cdot CNa(CO_2Et)_2 \\ \dot{C}H_2\cdot CNa(CO_2Et)_2 \end{matrix} + I_2 = 2NaI + \begin{matrix} CH_2\cdot C(CO_2Et)_2 \\ \dot{C}H_2\cdot \dot{C}(CO_2Et)_2. \end{matrix}$$

4. By intramolecular pinacone formation. Just as ketones on reduction yield pinacones:



$$\begin{matrix} (CH_3)_2\cdot C:O \\ (CH_3)_2\cdot C:O \end{matrix} + 2H = \begin{matrix} (CH_3)_2C\cdot OH \\ (CH_3)_2\dot{C}\cdot OH \end{matrix}$$

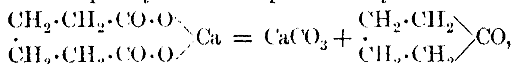
(cf. p. 198), so certain diketones on reduction yield cyclic pinacones, *i.e.* dihydric alcohols derived from the polymethylene hydrocarbons:



$$CH_2\begin{matrix} \diagup CH_2\cdot CO\cdot CH_3 \\ \diagdown CH_2\cdot CO\cdot CH_3 \end{matrix} + 2H = CH_2\begin{matrix} \diagup CH_2\cdot C(OH)\cdot CH_3 \\ \diagdown CH_2\cdot \dot{C}(OH)\cdot CH_3 \end{matrix}$$

1:2-Dimethyl-1:2-dihydroxy-cyclo-pentane.

5. A number of ketones derived from the polymethylenes have been obtained by the dry distillation of the calcium salts of the higher dibasic acids of the oxalic series (*J. Wislicenus*), *e.g.* calcium adipate yields keto-pentamethylene:



$$\begin{matrix} CH_2\cdot CH_2\cdot CO\cdot O \diagdown \\ \dot{C}H_2\cdot CH_2\cdot CO\cdot O \diagup \end{matrix} Ca = CaCO_3 + \begin{matrix} CH_2\cdot CH_2 \diagdown \\ \dot{C}H_2\cdot CH_2 \diagup \end{matrix} CO,$$

and this can be reduced to pentamethylene. The constitution of the keto-derivative follows from the fact that on oxidation the ring is ruptured and glutaric acid is formed. Keto-hexamethylene and keto-heptamethylene, suberone, have been obtained by similar methods, but the yields are poor. Ketones containing 16 or even 30 carbon atoms in the ring are formed by using thorium salts of dibasic acids of high molecular weight (Helv. 1926, 249, 499).

6. Hexamethylene compounds are often obtained by the catalytic reduction of benzene derivatives with nickel as catalyst. (Cf. Chap. XLIV, C.) This is a method of commercial importance as the following products obtained by this method are commercial solvents; cyclohexanol (sextol) from phenol, methylcyclohexanol from cresol, and these on oxidation yield respectively cyclohexanone (*sextone*) and methylcyclohexanone (*sextone B*). *Sextate* is cyclohexanyl acetate.

General Properties.—On the whole these compounds resemble

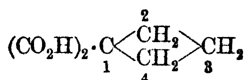
the paraffins as regards their chemical properties, hence the names cyclo-pentane for pentamethylene, cyclo-hexane, &c.

The trimethylene compounds, however, resemble the olefines, *e.g.* (*a*) they can combine with bromine to form additive compounds; (*b*) they are slowly oxidized by permanganate. In neither of these reactions do they take part so readily as the simpler olefines, and in all cases the products obtained are formed at the expense of the rupture of the ring.

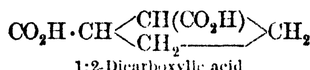
The fact that the majority of the hydrocarbons of this series resemble paraffins indicates that the formation of a closed chain does not affect to any considerable extent the properties of a compound (cf. Benzene).

In their chemical properties the compounds closely resemble the corresponding derivatives of the paraffins, *e.g.* the acids resemble to a large extent the fatty acids, yielding salts, esters, acid chlorides, amides, &c.

Isomerism.—(*a*) **Position Isomerism.**—No examples of isomerism have been met with in the case of mono-substituted derivatives, *e.g.* only one tetramethylenecarboxylic acid is known. Position isomerism can occur in the case of di- and poly-substituted derivatives, *e.g.* tetramethylene-1:1-dicarboxylic acid and isomeric 1:2 and 1:3 acids.



1:1-Dicarboxylic acid



1:2-Dicarboxylic acid



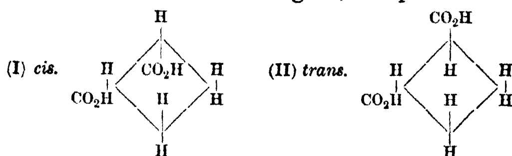
1:3-Dicarboxylic acid.

The number of isomerides possible in each case can be worked out by the student (cf. Benzene Derivatives).

(*b*) **Stereo-isomerism.**—Certain di-substituted derivatives have been found to exist in isomeric forms which are structurally identical. These must therefore be **stereo-isomeric.** Some of the simplest examples of this stereo-isomerism are met with in the dibasic acids. For example:

Tetramethylene-1:2-dicarboxylic acid exists in two isomeric forms. In both acids the $2CO_2H$ groups are attached to the carbon atoms 1 and 2, and the only difference is in the relative spatial relationships of the groups. If the plane of the paper represents the plane in which the centres of gravity of

the four carbon atoms of the ring lie, the possibilities are—



(I) That the two CO_2H groups lie in the same plane either above or below that of the paper (the *cis* acid); and (II) that the two CO_2H groups lie in different planes, one above and one below that of the paper (the *trans* acid). As a rule, the *cis* acids yield inner anhydrides, *e.g.* $C_4H_6{<}\begin{matrix}CO\\CO\end{matrix}{>}O$, more readily than the stereo-isomeric *trans* acids, and the *cis* acids are generally transformed into the corresponding *trans* acids when heated with hydrochloric acid at 190°. (*Perkin*, J. C. S. 1894, 572.)

A simple method of depicting these isomerides is due to *Aschan* (B. 1902, **35**, 3389). The plane of the carbon atoms of the ring is represented by a straight line. The unsubstituted hydrogen atoms are not denoted, only those which have been replaced by substituents. It has been found that the symmetry of such projections corresponds with the symmetry of the molecules projected. For the *cis* dicarboxylic acids, for example, if CO_2H = X, we have:



The *cis* compound (I) is not perfectly asymmetric, whereas the *trans* compound (II) is. Corresponding with (II) is a third isomeride, which stands in the same relationship to (II) as an object to its mirror image, or as *d*- to *l*-lactic acids. Both should therefore be optically active (one *d* and the other *l* to the same extent), and should be capable of combining to yield a racemic compound. All the *trans* compounds prepared artificially are optically inactive, and are presumably therefore racemic compounds of (II) and (III), and a few, *e.g.* *trans* trimethylene-1:2-dicarboxylic acid and the tricarboxylic acid, have been resolved into optically active components by means of quinine (B. 1905, 3102).

Cyclopentane-1:2:3-tricarboxylic acid (*Perkin* and *Robinson*, J. C. S. 1921, 1392) exists in two *meso* forms viz. *cis-trans-cis* and *cis-cis-cis* and a *racemic* form, *cis-trans-trans*, which can be resolved by brucine.

Intermediate between the polymethylene compounds and benzene derivatives are the reduction products of benzene and its derivatives, *e.g.* di- and tetra-hydrobenzene, tetrahydrophthalic acid, &c., C_6H_8, C_6H_{10}, $C_6H_8(CO_2H)_2$. These will be discussed along with the benzene compounds, from which they are derived.

XVII. BENZENE DERIVATIVES. INTRODUCTION

Benzene is, as its formula C_6H_6 shows, a compound much poorer in hydrogen than the paraffins, containing 8 hydrogen atoms less than hexane, C_6H_{14}; in the same way all benzene derivatives are much poorer in hydrogen, *i.e.* richer in carbon than the analogous methane derivatives, as is seen by comparing *e.g.* benzoic acid, $C_7H_6O_2$, with heptoic acid, $C_7H_{14}O_2$, or aniline, C_6H_7N, with ethylamine, C_2H_7N, &c.

The hydrogen atoms of benzene are, like those of methane, replaceable by numerous types of radicals. By the entrance of halogens, halide substitution products are formed, by the entrance of NH_2, aromatic bases, of OH, phenols, of NO_2, nitro-compounds, and of CH_3, &c., the homologues of benzene; there are, in addition to these, aromatic alcohols, aldehydes, acids, &c.

These benzene derivatives are partly analogous in their properties to the methane derivatives of corresponding composition; in part, however, they show new and peculiar properties of their own (see pp. 353 *et seq.*). One distinguishes between mono-, di-, tri-, &c., substituted benzene derivatives according as 1, 2, or more hydrogen atoms are replaced by the various radicals; thus, for instance, toluene, $C_6H_5 \cdot CH_3$, and chloro-benzene, $C_6H_5 \cdot Cl$, are mono-derivatives, dimethylbenzene, $C_6H_4(CH_3)_2$, and dichloro-benzene, $C_6H_4Cl_2$, di-derivatives, and so on. It is not necessary that the substituents should be identical, so that innumerable compounds are known containing various substituents, *e.g.* $OH \cdot C_6H_4 \cdot NO_2$, nitrophenol; $C_6H_4Br \cdot SO_3H$, bromobenzene-sulphonic acid; $CH_3 \cdot C_6H_3(NO_2)_2$, dinitro-toluene. Such compounds have usually some of the characteristics of all those mono-derivatives which result from benzene by the exchange of one hydrogen atom for one of these substituents.

All the derivatives of benzene can be converted either into benzene itself or into very closely allied compounds by *rela-*

tively simple reactions. Thus all the carboxylic acids of benzene (benzoic, phthalic, mellitic, &c.) yield benzene on distillation with lime, while other acids, such as salicylic, evolve CO_2 and yield phenol; the last-named compound is converted into benzene when distilled with zinc dust. The homologues of benzene are converted by oxidation into benzene-carboxylic acids, which yield benzene when heated with lime.

The relationship of a benzene derivative to its mother substance is therefore a very simple one.

This circumstance is one particularly worthy of note, since the atomic group C_6H_6 is already a tolerably complicated molecule in itself, and also because benzene cannot by any means be transformed into a simpler hydrocarbon containing 5, 4, or 3 carbon atoms; when oxidized, which is a matter of difficulty, it yields carbonic or similar simple organic acids.

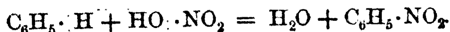
The benzene derivatives are connected with one another by the most varied reactions. The NO_2 group is readily convertible into NH_2, and the latter is replaceable by halogen, hydrogen, and hydroxyl; the halogen is also replaceable by methyl, carboxyl, &c.

As a rule, the group of 6 carbons with the hydrogens is spoken of as the **benzene nucleus**, and all substituents are spoken of as side chains. Thus in $C_6H_5 \cdot \underline{CHO}$, $C_6H_4 \cdot (\underline{CH_3})_2$, $C_6H_5 \cdot \underline{NH_2}$ the radicals underlined are the side chains.

A. Characteristic Properties of Benzene Derivatives

In many chemical properties benzene and its derivatives differ markedly from the paraffins or unsaturated open-chain hydrocarbons.

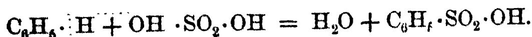
1. The aromatic hydrocarbons and their derivatives are readily attacked by concentrated nitric acid, yielding nitro-derivatives:



$$C_6H_5 \cdot H + HO \cdot NO_2 = H_2O + C_6H_5 \cdot NO_2.$$

Certain of the higher paraffins also yield nitro-derivatives when heated with nitric acid (p. 98).

2. Sulphonic acids are readily formed by the action of concentrated or fuming sulphuric acid:



$$C_6H_5 \cdot H + OH \cdot SO_2 \cdot OH = H_2O + C_6H_5 \cdot SO_2 \cdot OH.$$

This type of reaction is never met with in the aliphatic series.

3. The homologues of benzene differ from the paraffins especially as regards oxidation; while the latter are only attacked with difficulty by oxidizing agents, the former are readily converted into benzene-carboxylic acids:



$$C_6H_5 \cdot CH_3 \longrightarrow C_6H_5 \cdot CO_2H.$$

4. The halogens chlorine and bromine can react with benzene in two distinct ways: (*a*) yielding substituted derivatives, *e.g.* $C_6H_6 + Br_2 = C_6H_5Br + HBr$, or (*b*) yielding additive products, *e.g.* $C_6H_6Br_6$.

The process of substitution is the more important and the commoner of the two reactions.

5. There are not wanting other distinguishing characteristics between the aromatic hydrocarbons and the paraffins. Thus the halogen compounds C_6H_5X are chemically less active, and the hydroxyl compounds, *e.g.* $C_6H_5(OH)$, are of a more acidic nature than the corresponding fatty bodies. The phenyl radical, C_6H_5, is therefore more acid or "negative" in character than the ethyl, C_2H_5 (cf. *V. Meyer*, B. **20**, 534, 2944; A. **250**, 118).

6. Diazo-compounds are far more common in the aromatic series than in the aliphatic.

B. Isomeric Relations

1. While several isomeric mono-derivatives are both theoretically possible and have been actually obtained from each hexane, C_6H_{14}, benzene is only capable of forming a single mono-derivative in each case; isomeric mono-derivatives of benzene are unknown. *The six hydrogen atoms of benzene thus possess an equal value, or are similarly situated within the molecule.* This is not merely an empirical law, but one which has been proved experimentally.

PROOF OF THE EQUAL VALUE OF THE SIX HYDROGEN ATOMS

Let the 6 H atoms be designated as *a*, *b*, *c*, *d*, *e*, and *f* respectively.

(1) Phenol, $C_6H_5(OH)$, whose hydroxyl may have replaced the H atom *a*, may be converted into bromo-benzene, C_6H_5Br, and this latter into benzoic acid, $C_6H_5(CO_2H)$. The carboxyl in the latter has therefore also the position *a*, *i.e.* it has replaced the H atom *a*.

(2) Three hydroxy-benzoic acids, $C_6H_4(OH)(CO_2H)$, can either be prepared from benzoic acid or converted into it; their carboxyl therefore has the position *a*, and consequently their hydroxyl must replace some one of the other H atoms, be it *b*, *c*, or *d*.

(3) Each hydroxy-benzoic acid can be decomposed, yielding carbon dioxide and ordinary phenol, C_6H_5OH:



$$C_6H_4(OH)(CO_2H) = C_6H_5(OH) + CO_2.$$

And since the latter compound contains the hydroxyl in position *a*, according to (1), while the hydroxyl in the hydroxy-benzoic acids replaces the H atoms *b*, *c*, and *d*, it follows that the hydrogen atoms *a*, *b*, *c*, and *d* are of equal value.

(4) Now, as will be explained on p. 352, for each H atom there are present two other pairs of symmetrical hydrogen atoms, *i.e.* pairs of which either the one or the other atom may be replaced by any given radical without different substances resulting. But the atoms of such a pair cannot both be present in the positions *a*, *b*, *c*, and *d*, as in this case three hydroxy-benzoic acids could not exist. It must therefore be the remaining H atoms *e* and *f* which are respectively in positions symmetrically situated to two of the former, and which are therefore of equal value with them, *i.e.* $e = c$, $f = b$. Since, however, $a = b = c = d$, it follows that all the 6 hydrogen atoms are of equal value (*Ladenburg*, B. 7, 1684).

2. With di-substituted derivatives of benzene it has been found that in each case three distinct isomeric forms exist. The two substituents may be alike, or they may be dissimilar, *e.g.* three dichloro-benzenes, $C_6H_4Cl_2$, three diamino-benzenes, $C_6H_4(NH_2)_2$, three dimethyl-benzenes, $C_6H_4(CH_3)_2$, three hydroxy-benzoic acids, $C_6H_4(OH)(CO_2H)$, are known. In no case have more than three such isomerides been found.

It can be shown that with respect to each H atom of benzene, *e.g.* for *a*, two pairs of other H atoms, *e.g.* *b* and *f*, *c* and *e*, are symmetrically situated, so that it makes no difference whether, after *a* is replaced, the second substituent replaces the one or the other of the symmetrically placed hydrogen atoms, say *b* or *f*. According to the above notation, therefore, $ab = af$, and $ac = ae$. On the other hand, the combinations *ab* and *ac* are not equivalent, but represent isomers; the combination *ad*, the only remaining case, represents the third isomer.

PROOFS THAT FOR EVERY H ATOM (*a*) TWO OTHER PAIRS OF SYMMETRICALLY LINKED H ATOMS EXIST

1. According to *Hübner* and *Petermann* (A. **149**, 129; cf. also *Hübner*, A. **222**, 67, 166), the (so-called meta-) bromobenzoic acid, which is obtained by brominating benzoic acid, and whose Br atom may be in position *c* and CO_2H in position *a*, yields with nitric acid two nitrobromo-benzoic acids, $C_6H_3Br(NO_2)(CO_2H)$, the NO_2 being, say, in positions *b* and *f*. These are both reduced by nascent hydrogen to the same (so-called ortho-) amino-benzoic acid, $C_6H_4(NH_2)(CO_2H)$, the NO_2 being here changed to NH_2 and the Br replaced by H. Since the same amino-benzoic acid is formed in both cases, notwithstanding that the nitro-groups must be in the place of different H atoms, say *b* and *f*, from the fact of the two nitro-acids being dissimilar, it follows that *b* and *f* must be arranged symmetrically as regards the H atom *a*, *i.e.* *ab* = *af*.

2. In an analogous manner salicylic acid, $C_6H_4(OH)(CO_2H)$, which can be prepared from the above-mentioned amino-benzoic acid, yields two nitro-derivatives, $C_6H_3(OH)(NO_2)(CO_2H)$. If, however, the hydroxyl in these is replaced by hydrogen (a reaction which can be effected by indirect methods), the nitrobenzoic acids thus obtained, $C_6H_4(NO_2)(CO_2H)$, are identical, and therefore the H atoms which have been replaced by NO_2 are in positions symmetrical to *a*. When this nitrobenzoic acid is in its turn reduced to amino-benzoic acid, $C_6H_4(NH_2)(CO_2H)$, it is not the above (ortho-) amino-acid (where *ab* = *af*) which is obtained, but an isomer. The NO_2 groups cannot therefore here be in the positions *b* and *f*, but must replace two other H atoms which are likewise symmetric towards *a*, say *c* and *e*, *i.e.* *ac* = *ae* (*Hubner*, A. **195**, 4).

Thus two pairs of H atoms are symmetrically situated as regards the H atom *a*: *ab* = *af*; *ac* = *ae*. The only other possible combination is *ad*, *i.e.* the sixth H atom has no other H atom corresponding with it relatively to *a*.

Nöelting (B. 1904, **37**, 1015) has shown that the 2-chloro-6-hydroxy-toluene and the 6-chloro-2-hydroxy-toluene obtained by the following reactions are identical:

1. 6-nitro-2-amino-toluene ⟶ 6-nitro-2-chloro-toluene ⟶ 6-amino-2-chloro-toluene ⟶ 6-hydroxy-2-chloro-toluene.
2. 6-nitro-2-amino-toluene ⟶ 6-nitro-2-hydroxy-toluene ⟶ 6-amino-2-hydroxy-toluene ⟶ 6-chloro-2-hydroxy-toluene.

Cf. also *Cohen*, J. C. S. 1915, **107**, 847.

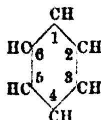
It has been assumed in the considerations just detailed that when one compound is converted into another by the exchange of atoms or radicals (NH_2 for NO_2, H for OH), this exchange is effected without a so-called "molecular rearrangement" taking place at the same time (see p. 138). Experience has proved that this may be taken for granted in a large number of reactions which proceed with relative smoothness and at comparatively low temperatures. Those instances in which a molecular rearrangement ensues are now well known; especially is this the case in the fusion of sulphonic acids with potash (exchange of SO_3H for OH), a reaction which takes place at relatively high temperatures only, and which frequently leads to isomers of the compounds expected. Other examples are: (*a*) potassium ortho-hydroxy-benzoate heated at 200° yields the potassium salt of the para-acid; (*b*) all three isomeric bromo-benzene-sulphonic acids, $C_6H_4Br \cdot SO_3H$, and the three bromo-phenols, $C_6H_4Br \cdot OH$, yield resorcinol or meta-dihydroxy-benzene, *m*-$C_6H_4(OH)_2$, when fused with potash; (*c*) ortho-phenol-sulphonic acid when heated yields the isomeric para-acid, *p*-$OH \cdot C_6H_4 \cdot SO_3H$. Reactions of this nature probably arise from the successive taking up and splitting off of atoms or atomic groups.

CONSTITUTION OF BENZENE

The formula C_6H_6 at once indicates that benzene cannot be a saturated open-chain compound. The possibility that it is an open-chain unsaturated compound containing several double or triple bonds has been shown to be untenable, *e.g.* dipropargyl (p. 56), $CH\vdots C \cdot CH_2 \cdot CH_2 \cdot C\vdots CH$, although resembling benzene in physical properties, is quite different as regards most of its chemical properties; it combines readily with bromine, yielding additive compounds with 2, 4, 6, or 8 atoms of bromine, and it is also oxidized with the greatest readiness. Benzene combines with bromine only slowly and under specific conditions, and then yields $C_6H_6Br_6$; it is, further, extremely stable towards oxidizing agents. The equivalency of the 6 hydrogen atoms in the benzene molecule is a further strong argument against such open-chain formulæ. *Kekulé* was the first to suggest a closed-chain, cyclic, or ring formula for benzene.

In order to account for the existence of only one mono-substituted derivative, C_6H_5X, but of three isomeric di-sub-

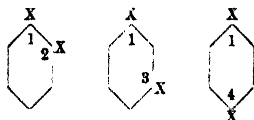
stituted derivatives, $C_6H_4X_2$, it is necessary to assume that a single hydrogen atom is attached to each carbon atom.



This formula is usually known as the benzene ring.

In the above formula the six hydrogen atoms are symmetrically placed with respect to one another, and thus in the formation of a mono-substituted derivative it is immaterial which one of the six hydrogens is replaced; only one compound, C_6H_5X, can be formed.

With di-substituted derivatives three isomerides are theoretically possible, viz.:

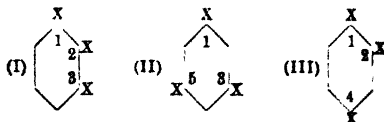


the 1:2 or ortho-compound, 1:3 or meta-compound, and the 1:4 or para-compound.

The compound 1:5 is identical with 1:3, and 1:6 is identical with 1:2. Cf. *Wohl*, B. 1910, **43**, 3474.

The hydrogen atoms in positions 2:6 form one pair of symmetrical hydrogen atoms mentioned on p. 356, and those in positions 3:5 form the second pair, whereas the hydrogen in position 4 has no other hydrogen atom corresponding with it.

Similarly, three tri-substituted derivatives, $C_6H_3X_3$, are known, and only three are possible with such a ring formula, viz.:

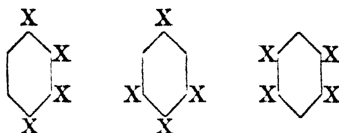


(I) 1:2:3 or adjacent tri-derivative.
(II) 1:3:5 or sym. tri-derivative.
(III) 1:2:4 or unsym. tri-derivative.

Any other combination is identical with one of these, 2:4:6 = 1:3:5, and 1:4:6 = 1:2:4.

The number of isomerides is considerably increased when the three substituents are not similar, *e.g.* in a compound, $NH_2 \cdot C_6H_3Br \cdot CO_2H$.

With a tetra-substituted derivative, $C_6H_2X_4$, where all four substituents are alike, only three isomerides are possible, namely those corresponding with the *o*-, *m*-, and *p*-di-derivatives:

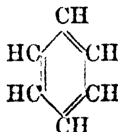


And with a penta-substituted derivative, C_6HX_5, only one form is possible.

The number of isomerides actually found in each case is in perfect harmony with these theoretical deductions.

The ring formula for benzene, given above, represents each carbon atom as tervalent; the difficulty of accounting for the fourth valency can be overcome in several ways.

The first method, suggested by *Kekulé*,* was to suppose alternate double and single bonds between the 6 carbon atoms, *e.g.*:

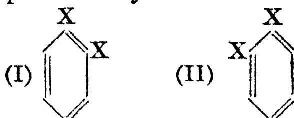


This formula is in perfect harmony with the formation of benzene from acetylene, and of trimethyl-benzene from acetone. It also largely accounts for the formation of additive compounds by benzene and its derivatives, *e.g.* di-, tetra- and hexa-hydro-derivatives, C_6H_8, C_6H_{10}, C_6H_{12} (p. 377); benzene hexachloride, $C_6H_6Cl_6$ (p. 382); the triozonide, $C_6H_6O_9$ (Chap. XLV, F.), and an additive compound with ethyl diazoacetate.

Two arguments which have been brought forward against this formula are—

* This formula was suggested by *Loschmidt* four years before it was enunciated by *Kekulé* (cf. B. 1912, **45**, 539).

(*a*) Two ortho-disubstituted derivatives should be possible, namely, those represented by the formulæ:

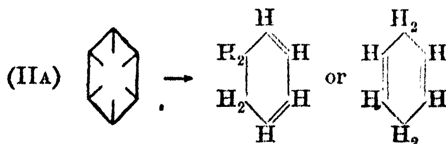


In formula (I) the 2 carbon atoms to which the substituents are attached are united by a double bond, and in formula (II) by a single bond. *Kekulé* has suggested that the single and double bonds may be continually changing, so that positions 2 and 6 are really symmetrical with respect to 1.

(*b*) The stability of benzene towards oxidizing agents has been used as an argument against such a formula containing three double bonds in the molecule. Di- and tetrahydro-benzenes—obtained by the reduction of benzene—which contain respectively two and one double bonds in their molecules, are readily oxidized, and also readily yield additive compounds with halogens. They also give quite different ultra-violet absorption spectra. Evidence based on other physical constants, such as molecular refraction, molecular volumes, molecular magnetic rotations, and heats of combustion, is inconclusive and conflicting. It has been suggested that the peculiar symmetrical structure of the benzene molecule may account for its stability, but the fact that cyclo-octa-tetrene, C_8H_8 (Chap. LVI), which contains 8 CH groups united alternately with double and single linkings, has the properties of an olefine and not of an aromatic compound, is a strong argument against the *Kekulé* formula. (*Willstätter*, B. 1911, **44**, 3423; 1913, **46**, 517.)

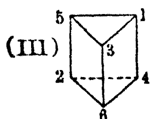
(II) A second method of accounting for the fourth valency of each carbon atom is that first suggested by *Armstrong*, and afterwards developed by *Baeyer*, centric formula (IIA).

It represents the fourth valency of each carbon atom as directed towards the centre of the molecule, where the **6** are kept in equilibrium, a method of linking which is unknown in the fatty series. When reduced to dihydro-benzene, four of the six centric bonds form two double bonds.

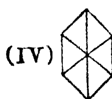


This readily accounts for the great difference between the chemical properties of benzene and of its reduction products.

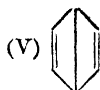
Various other formulæ have been suggested for benzene, *e.g.* *Ladenburg's* prism formula, *Claus's* diagonal formula, and *Dewar's* formula. For *Thiele's* formula, see Chap. L, C.



Ladenburg



Claus



Dewar

A strong objection to the prism formula and to any other three-dimension space formula is that the molecules of certain substituted derivatives would be perfectly asymmetric, and should therefore exist in optically active modifications. No benzene derivative which occurs naturally is optically active, and attempts to resolve substituted benzene derivatives, *e.g.* $C_6H(OH)(CO_2H)(CH_3)(C_3H_7)(NO_2)$, nitrothymotic acid, have been unsuccessful. *Rugheimer* (B. 1896, **29**, 1967) states, however, that he has obtained *m*-methyl-*p*-hydroxy-benzoic acid in an optically active form.

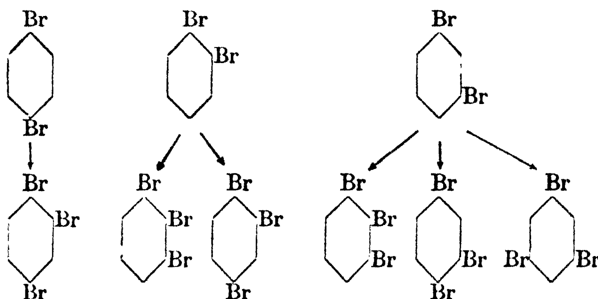
Other objections to the prism formula are (*a*) the difficulty of accounting for the reduction products of benzene, and (*b*) the fact that when benzene is oxidized by various methods no compound is met with which contains a carbon atom attached to 3 other carbon atoms, as is the case in the prism formula.

As the result of a number of researches *Baeyer* came to the conclusion that a ring-structure characteristic of benzene itself need not be valid for all its derivatives; some may have olefinic, others centric structures.

For full discussion on the benzene ring problem, cf. *Kauffmann*, Ahrens Sammlung, 1907, **12**, 79; *Pauly*, J. pr. 1918, **98**, 106; and for an explanation based on continuous oscillation of atoms within the molecule, cf. *Von Weinberg*, B. 1919, **52** B., 928. Formulæ based on the theory of electrons have been put forward by *Fry*, J. A. C. S. 1912, **34**, 664; 1914, **36**, 248, 262, 1035; 1915, **37**, 855, 2368; 1916, **38**, 1323; 1917, **39**, 1688; *J. J. Thomson*, Phil. Mag. 1914, **27**, 784; *Pauly*, J. pr., 1918, [ii], **98**, 118; *Kermack* and *Robinson*, J. C. S. 1922, 437; *Huggins*, J. A. C. S. 1922, 1607; *Crocker*, ibid. 1618.

METHODS FOR DETERMINING WHICH OF THREE ISOMERIC COMPOUNDS IS THE ORTHO, WHICH META, AND WHICH PARA.

1. A method worked out by *Körner* (1875) for the three dibromobenzenes. One of these (*a*) is a solid melting at 89°; a second (*b*) is a liquid which boils at 224°, and when solidified melts at −1°; and the third (*c*) is a liquid boiling at 219° and melting at +1°. When further brominated, the compound *a* yields only *one* tribromobenzene; compound *b*, under similar conditions, yields a mixture of *two* isomeric tribromobenzenes; and compound *c* a mixture of *three.*



From a glance at the above formulæ, it is obvious (1) that the para- or 1:4-compound could give rise to only *one* tribromobenzene, (2) that the ortho- or 1:2-compound could give a mixture of *two* isomeric tribromobenzenes, and (3) that the meta- or 1:3-compound could give a mixture of *three* isomeric tribromobenzenes.

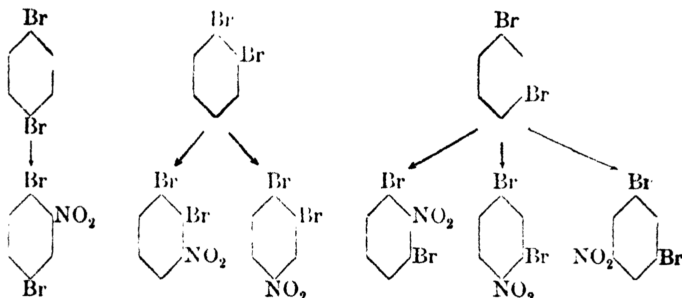
The compound melting at 89° is therefore *p*-dibromobenzene, the one boiling at 224° is the ortho-, and the one boiling at 219° and melting at +1° is the meta-compound.

Incidentally, this gives us a method for determining which of the three tribromobenzenes is the adj., which the sym., and which the unsym. A glance at the formulæ indicates that the sym.-tribromobenzene is the one which is formed from the *m*-dibromobenzene only. The adj. is the one formed from both ortho- and meta-, and the unsym. is the one which is formed from ortho-, meta-, and para-dibromobenzenes.

Similar results are obtained by examining the nitro-dibromobenzenes obtained by nitrating the dibromobenzenes.

The *p*-compound yields only one nitro-derivative; the *o*-com-

pound yields two nitro-derivatives; the *m*-compound yields three nitro-derivatives:



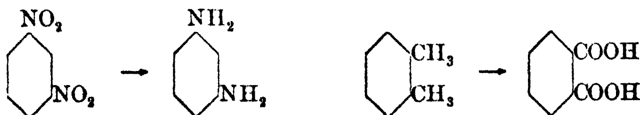
but the nitro-dibromobenzenes thus formed are all different.

Similar methods may be adopted for determining the constitutions of the three diamino-benzenes, $C_6H_4(NH_2)_2$, by determining from how many of the six diamino-benzoic acids each of the three can be obtained by elimination of carbon dioxide.

The *m*-compound is the one which is formed from three distinct acids, the ortho- from two, and the para- from one only (*Griess*).

The relationships between the three xylenes, $C_6H_4(CH_3)_2$, and the six nitro-xylenes are exactly analogous to those between the three dibromobenzenes and their six nitro-derivatives.

2. When the constitution of several groups of compounds, *e.g.* the dibromobenzenes, the xylenes, and the diamino-benzenes have been settled, then the constitutions of other compounds can be determined by conversion into one of the compounds of known constitution, *e.g.* the dinitro-benzene which yields *m*-diamino-benzene on reduction is the *m*-dinitro-compound, or the acid obtained by the oxidation of *o*-xylene must be the *o*-dicarboxylic acid.



This constitution is confirmed by the fact that this acid is the only one of the three isomeric benzene-dicarboxylic

acids which yields an inner anhydride, phthalic anhydride, $C_6H_4<\genfrac{}{}{0pt}{}{CO}{CO}>O$, and hence the two CO_2H groups are probably attached to two adjacent carbon atoms.

3. The constitution of certain di-substituted derivatives is based on *Ladenburg's* proof (A. 179, 174) of the equivalence of the three unsubstituted hydrogen atoms in mesitylene, $C_6H_3(CH_3)_3$; in other words, on the fact that mesitylene is sym.-trimethyl-benzene, *e.g.* the constitution of *m*-xylene is based on the following reactions:—

[Benzene ring diagrams: ring with CH_3 at top and CH_3 at lower left and lower right → ring with CH_3 at top, CO_2H at lower left and CH_3 at lower right → ring with CH_3 at top and CH_3 at lower right]

Ladenburg's proof is briefly as follows:—Mesitylene yields a dinitro-derivative, $C_6H(CH_3)_3(NO_2)_2$, in which two of the three nucleus hydrogen atoms (*a* and *b*) are replaced by nitro-groups. From this we get, by the three processes of reduction, acetylation, and nitration, a dinitro-acetamino-mesitylene:

$$C_6H(CH_3)_3\underset{a}{(NO_2)}\underset{b}{(NH_2)} \rightarrow C_6H(CH_3)_3(NO_2)(NHAc)$$
$$\rightarrow C_6(CH_3)_3(NO_2)_2(NHAc),$$

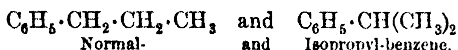
in which the third hydrogen (*c*) is replaced by NO_2; on hydrolysis, this yields $C_6(CH_3)_3(NO_2)_2(NH_2)$, and on elimination of the amino-group, $C_6H(CH_3)_3(NO_2)_2$, a dinitro-mesitylene, which is identical with the original dinitro-compound started with. Hence two of the hydrogen atoms (say *b* and *c*) are similarly situated. The nitro-amino-mesitylene, $C_6H(CH_3)_3\underset{a}{(NO_2)}\underset{b}{(NH_2)}$, in which the nitro-group is in position *a* and the amino- in position *b*, yields $C_6H_2(CH_3)_3\underset{a}{NO_2}$, and this, when reduced, acetylated, nitrated, and hydrolysed:

$$C_6H_2(CH_3)_3\underset{a}{NH_2} \rightarrow C_6H_2(CH_3)_3\cdot\underset{a}{NHAc}$$
$$\rightarrow C_6H(CH_3)_3\underset{a}{(NHAc)}\underset{b \text{ or } c}{(NO_2)} \rightarrow C_6H(CH_3)_3\underset{a}{(NH_2)}\underset{b \text{ or } c}{(NO_2)},$$

a nitro-amino-mesitylene which is identical with the original nitro-amino-mesitylene, and hence the position *a* is similarly situated to either *b* or *c*, but in the first part of the argument it was shown that $b = c$, $\therefore a = b = c$.

Other Types of Isomerism.—1. In addition to the cases of isomerism dealt with in the preceding pages (isomerism due to the positions of the substituents in the nucleus), other types of isomerides are met with. A frequent example is the isomerism of a compound containing a substituent in the nucleus with a compound containing the same substituent in the side chain; well-known examples are $C_6H_4Cl \cdot CH_3$ and $C_6H_5 \cdot CH_2Cl$, $C_6H_4{<}^{CH_3}_{NH_2}$ and $C_6H_5 \cdot CH_2 \cdot NH_2$. Isomerism of this type is usually accompanied by considerable difference in chemical properties.

2. "Side-chain isomerism" is the name given when the isomerism is confined to the side chain, *e.g.*:



$C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CH_3$ and $C_6H_5 \cdot CH(CH_3)_2$
Normal- and Isopropyl-benzene.

Stereo-isomerism.—When the side chain contains an asymmetric carbon atom, *e.g.* $C_6H_5 \cdot CH(OH)(CO_2H)$, mandelic acid, stereo-isomerism of the type of the active lactic acids is met with. Stereo-isomerism of the type of the crotonic acids is met with in unsaturated compounds like cinnamic acid, $C_6H_5 \cdot CH{:}CH \cdot CO_2H$, and stereo-isomerism analogous to that described in the case of polymethylene derivatives is met with among the reduced benzene derivatives, *e.g.* di-, tetra-, and hexahydrophthalic acid (p. 498).

OCCURRENCE OF THE BENZENE DERIVATIVES

Many benzene derivatives occur in nature, *e.g.* oil of bitter almonds, benzoic acid, salicylic acid, and hippuric acid, while others are obtained from the destructive distillation of organic substances, especially of coal.

The destructive distillation of coal yields (*a*) gases (illuminating gas); (*b*) an aqueous distillate containing ammonia and its salts, &c.; (*c*) coal-tar; and (*d*) coke.

Coal-tar.—Coal-tar is the chief source of benzene derivatives, and is formed in the manufacture of coal-gas for illuminating purposes, and in "coke ovens" used for the production of high-grade coke for metallurgical purposes. In both cases coal is distilled from closed retorts at relatively high temperatures, about 1000° C., and the main difference between the two processes is the nature of the coal used. For gas-making a bituminous coal containing 32–40 per cent of

volatile matter is used, and in order to obtain the maximum yield of hard coke bituminous coals containing from 18–32 per cent of volatile matter are employed.

The yields of products per ton of coal can be taken as:

	Gasworks.		Coke Ovens.
Gas	10,000–12,000 cu. ft.	= 17 %	10·6 %
Ammoniacal liquor	177 lb.	= 7·9 %	9·0 %
Tar	10 gall.	= 5·0 %	4·0 %
Coke	0·7 ton	= 70·0 %	71·5 %

The tar from the two processes is much the same.

At the present time numerous low-grade coals, *e.g.* cannel coal, lignite or brown coal, and even bituminous shales, are distilled at comparatively low temperatures (500–600° C.) in order to obtain oils, and, in the case of cannel coals, smokeless fuel for household purposes, **coalite**. The tar produced in all these cases is essentially different from the coal-tar obtained from gasworks and coke ovens. It consists largely of paraffin hydrocarbons, and is valueless for the manufacture of dye-stuffs, explosives, &c., but yields valuable illuminating and fuel oils.

When coal-gas was first generally used for illuminating purposes (1813) the tar was regarded as a waste product, and could only be used as fuel, and its value as the source from which important synthetic dyes, perfumes, explosives, medicinal drugs, and photographic developers could be manufactured was only gradually recognized. For many years after the introduction of coke ovens for the manufacture of metallurgical coke, the ammonia and tar formed at the same time were not collected (so-called bee-hive ovens), but at the present time the great majority of the ovens are of the closed type, and are provided with by-product recovery plant. Still more recently, as the demand for benzene and toluene has increased, it has become customary to recover the benzene and toluene contained in the gas from the coke ovens, and even from the gas from gasworks, although this removal appreciably diminishes the illuminating power of the gas. The benzene hydrocarbons are usually removed by passing the gas through scrubbers containing creosote oil, which absorbs the hydrocarbons, and these can be afterwards isolated by heating the creosote oil or subjecting it to steam distillation. The amount of benzene and toluene in coal-gas is, roughly,

about 15 times as much as that contained in the tar formed at the same time. In coke-oven gases the amount is only about half this. By this method of extracting benzene and toluene from the gases the amounts of these materials for the manufacture of explosives, &c., has been increased enormously.

The following figures will give some idea of the importance of the coal-tar industry:—

In 1914, in Great Britain, about 14·5 million tons of coal were coked in by-product coking plants, and about 20 million tons distilled in gasworks. In the U.S.A. about 20 million tons were treated in recovery coke ovens, and about 20 million tons in gasworks.

In the U.S.A. the output of crude benzol was about 4·5 million gallons in 1914, and this was increased to 40 million gallons in 1917.

Coal-tar contains as many as 200 different chemical sub stances; these are not present in the coal itself, but are formed during the distillation. During the past thirty years investigators have attempted to isolate compounds from coal itself by extraction with solvents, such as chloroform (*Keinsch*, 1910), pyridine (*Bedson*, 1908), benzene (*Pictet* and *Ram*, 1911), but so far few relationships have been established between the different materials present in coal and the chemical compounds present in tar (cf. *Tideswell* and *Wheeler*, J. C. S. 1919, **115**, 619).

The most important compounds present in coal-tar are benzene, toluene, xylenes, phenol, cresols, naphthalene, and anthracene. Among the other compounds present are homologues of benzene, especially the methyl homologues; complex hydrocarbons, such as diphenyl, phenanthrene, fluorene, acenaphthene, chrysene and retene, indene and its homologues, and homologues of naphthalene; thiophene, benzointrile, aniline, pyridine and its homologues; quinoline, isoquinoline, pyrrole, indole, carbazole, and acridine. Most of these are of little commercial importance, as the amounts present are small and their isolation from the tar is difficult.

Many of the hydrocarbons present in the tar are probably formed by the pyrogenic polymerization of acetylene, as this hydrocarbon when heated yields many of the products present in coal-tar (*R. Meyer* and *H. Fricke*, B. 1914, **47**, 2765).

The crude tar contains appreciable amounts of water, and has to be dehydrated before it can be distilled. Numerous methods are adopted, *e.g.* centrifuging the warm tar; heating

the tar, allowing the water to rise to the surface, and removing it by a draw-off cock; or allowing the wet tar to come in contact with the hot vapour from another lot of boiling dehydrated tar.

The actual distillation is carried out in iron stills directly fire-heated. In many tar distilleries continuous stills are employed; in others intermittent distillation is used, the pitch being removed and a fresh charge of tar introduced from time to time.

The fractions collected vary in different distilleries, but, as a rule, in the first distillation the following are collected:—(1) First runnings up to 105° or 110°; this contains water, ammonia, and some light oil. (2) Light oils up to 210°. (3) Middle oil or carbolic oil up to 240°. (4) Creosote oil up to 270°. (5) Anthracene oil above 270°. (6) Residue in the still = pitch.

The relative amounts of the different fractions vary considerably in different countries and different districts, but the following are fairly typical values for 1 ton of tar:—Light oils, 12 gall.; carbolic oil, 20 gall.; creosote oil, 17 gall.; anthracene oil, 38 gall.; and pitch, 11 cwt. Calculated on 1 ton of tar, the yields of important products are:—Benzene and toluene, 25 lb., or 1·1 per cent; phenol, 11 lb., or 0·5 per cent; cresols, 50 lb., or 2·2 per cent; naphthalene, 180 lb., or 8 per cent; creosote, 200 lb., or 8·8 per cent; and anthracene, 6 lb., or 0·27 per cent.

The light oils, including those from the first runnings, give rise to 60–65 per cent of benzene hydrocarbons, 12–15 per cent of naphthalene, 8–10 per cent of phenols, and 1–3 per cent of pyridine bases. The phenols are readily removed by treatment with caustic soda solution, and the pyridine bases by treatment with dilute mineral acids. The neutral substances, on further fractionation under varying conditions, yield 90 per cent benzol, 50 per cent benzol, 30 per cent benzol, and solvent naphtha. The numbers 90, 50, and 30 denote the percentage of the oil which passes over below 100° C., and not the actual benzene content of the oil. 90 per cent benzol contains 81 per cent of benzene, 15 per cent of toluene, 2 per cent of xylenes, and 2 per cent of impurities; and 30 per cent benzol contains respectively 13·5, 73·4, 11·7, and 11·7 per cent. From these crude benzols, by careful fractionation, pure benzene, toluene, and xylenes can be isolated.

In addition to the compounds, such as benzene, toluene, naphthalene, phenol, and anthrace, which are actually isolated and form important articles of commerce, a number of products consisting of complex mixtures are also manufactured. The most important of these are (1) solvent naphtha, which is used as a solvent for rubber in preparing waterproof fabrics and also for burning purposes, and (2) creosote oil, which is used in enormous quantities for pickling timber for use as railway sleepers, posts, and other purposes.

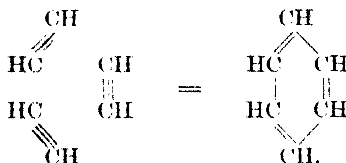
For hydrogenation of coal cf. *Bergius*, Chem. Age, 1927, 134.

Hexahydro-compounds of benzene and its homologues have been found in most natural petroleums, especially in those from the Caucasus (J. pr. Ch. (2) **45,** 561; cf. p. 41).

FORMATION OF BENZENE DERIVATIVES FROM OPEN-CHAIN COMPOUNDS

The benzene derivatives can be produced from the fatty compounds by a relatively small number of reactions only.

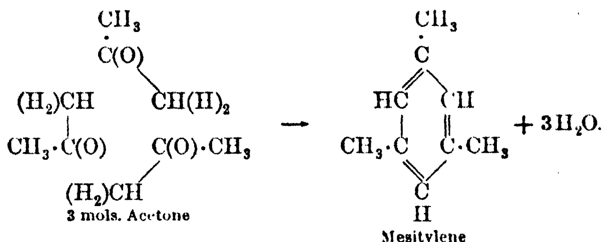
1. Many methane derivatives, *e.g.* alcohol, yield a mixture containing a large number of the derivatives of benzene when their vapours are led through red-hot tubes. Acetylene, C_2H_2, polymerizes at a low red heat to benzene, C_6H_6 (*Berthelot*):



In an analogous manner allylene, $CH_3\cdot C\vdots CH$, yields mesitylene or 1:3:5 trimethyl-benzene, $C_6H_3(CH_3)_3$, when distilled with dilute sulphuric acid, while crotonylene, $CH_3\cdot C\vdots C\cdot CH_3$, yields hexamethyl-benzene, $C_6(CH_3)_6$; bromo-acetylene and iodo-acetylene polymerize to *s*-tribromo- and tri-iodo-benzene when exposed to light; propiolic acid, $CH\vdots C\cdot CO_2H$, polymerizes to trimesic acid, $C_6H_3(CO_2H)_3$.

2. Natural gas, consisting largely of ethane and propane, when subjected to the process of "cracking" (p. 43), especially in the presence of metals, at various temperatures gives rise to aromatic hydrocarbons, and it has been suggested that these are the result of the following series of changes: ethane ⟶ ethylene ⟶ butadiene ⟶ benzene (J. I. E. C. 1918, **10,** 901).

3. Ketones condense to benzene hydrocarbons when distilled with dilute sulphuric acid, *e.g.* acetone yields mesitylene (*Kane*, 1838) and methylethyl ketone, triethyl-benzene:

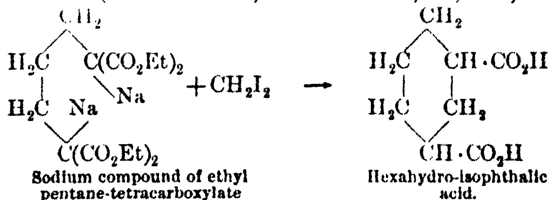


Hydroxy-methylene-acetone (p. 232) readily undergoes condensation, yielding triacetyl-benzene.

4. Certain 1:2-diketones, aldehyde acids, and keto-aldehydes are transformed in an analogous manner into benzene derivatives by suitable "condensing" agents; diacetyl, $CH_3\cdot CO\cdot CO\cdot CH_3$, is transformed by alkalis into xylo-quinone, $C_6H_2O_2(CH_3)_2$ (B. **21**, 1411), and ethyl β-hydroxyacrylate into the ethyl ester of trimesic acid (B. **20**, 2930).

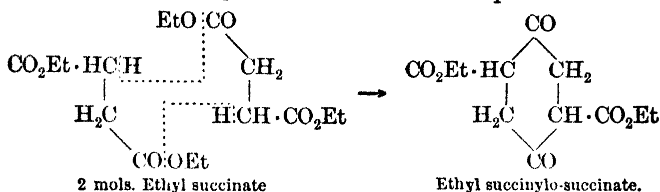
5. Certain 1:5 diketones react with hydrochloric acid, yielding reduced benzene derivatives, which can readily be transformed into benzene derivatives, *e.g.* ethylidene-diacetoacetic ester (from acetaldehyde and acetoacetic ester) yields dimethyl-cyclo-hexenone, $CH\lessgtr\genfrac{}{}{0pt}{}{CO-CH_2}{CMe\cdot CH_2}\gtrless CHMe$, the dibromide of which is converted into sym.-xylenol, $CH\lessgtr\genfrac{}{}{0pt}{}{C(OH):CH}{CMe-CH}\gtrless CMe$ (*Knoevenagel*).

6. By the hydrolysis of the product from methylene iodide and ethyl sodio-pentane tetracarboxylate, hexahydro-isophthalic acid is formed (*W. H. Perkin*, J. C. S. 1891, **59**, 798):



7. By the action of sodium upon ethyl succinate (*Herrmann*, A. **211**, 306; B. **16**, 1411), or upon ethyl bromo-acetoacetate (*Duisberg*), **ethyl succinylo-succinate**, "ethyl cyclo-hexan-2:5-

dione-1:4-diacid", is obtained, and is readily transformed into ethyl dihydroxy-terephthalate and then into quinol:



2 mols. Ethyl succinate — Ethyl succinylo-succinate.

8. When ethyl sodio-malonate, $CHNa(CO_2Et)_2$, is heated, ethyl phloroglucinol-dicarboxylate is formed, and this on hydrolysis yields phloroglucinol, which is also formed from malonyl chloride and acetone in the presence of calcium carbonate.

9. Hexyl iodide, $C_6H_{13}I$, is converted into hexachloro-benzene, C_6Cl_6, when heated with ICl_3, and into hexabromo-benzene, C_6Br_6, by bromine at 260°; the latter compound can also be obtained by heating CBr_4 to 300°.

10. **Mellitic acid**, $C_6(CO_2H)_6$, is produced by the oxidation of graphite or lignite by means of $KMnO_4$.

11. **Potassium carboxide**, which is formed by the action of carbon monoxide upon potassium, is the potassium compound of hexahydroxy-benzene, $C_6(OH)_6$.

12. For the conversion of hydroaromatic compounds into benzene derivatives, see *Crossley* and others, J. C. S. 1903, **83**, 110; 1904, **85**, 264; 1906, **89**, 875; 1914, **105**, 165.

THE CONVERSE TRANSFORMATION OF BENZENE DERIVATIVES INTO FATTY COMPOUNDS

1. When the vapour of benzene is passed through a red-hot tube it is partially decomposed into acetylene.

2. Benzene is oxidized by chloric acid to "**trichloro-phenomalic acid**", *i.e.* β-trichloraceto-acrylic acid, $CCl_3 \cdot CO \cdot CH:CH \cdot CO_2H$ (*Kekulé* and *Strecker*, A. **223**, 170).

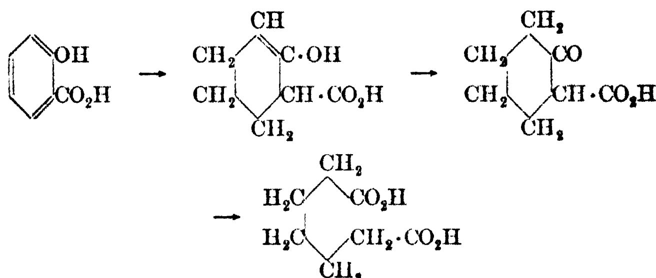
When chlorine is allowed to act upon phenol in alkaline solution, the benzene ring is broken, and the acids, $C_6H_5Cl_3O_4$, $C_6H_5ClO_4$, &c., are produced (*Hantzsch*, B. **20**, 2780). Catechol, resorcinol, and phloroglucinol are also ultimately converted into fatty compounds by treatment with chlorine and the subsequent action of alkalis, *e.g.* resorcinol (*m*-dihydroxy-benzene) yields dichloro-maleic acid (B. 1894, **27**, 3364). Bromine, acting upon bromanilic acid, yields perbromo-acetone, $CBr_3 \cdot CO \cdot CBr_3$.

3. Nitrous acid and catechol yield dihydroxy-tartaric acid (p. 269), and phenol and potassium permanganate yield tartaric and oxalic acids.

4. Oxidizing agents which are capable of rupturing the benzene ring yield, as a rule, carbonic, formic, and acetic acids.

5. The hexahydro-benzenes are transformed with difficulty into hydrocarbons of the methane series when heated with hydriodic acid at 280° (*Berthelot*, A. **278**, 88; **302**, 5).

6. When reduced with metallic sodium and amyl alcohol, *o*-hydroxy-benzoic acid is converted into pimelic acid:

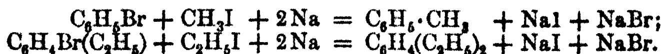


XVIII. BENZENE HYDROCARBONS

A. Homologues of Benzene, C_nH_{2n-6}

The benzene hydrocarbons are for the most part colourless liquids, insoluble in water, but readily soluble in alcohol and ether (durene and penta- and hexamethyl-benzenes are crystalline). They distil without decomposition, possess a peculiar and sometimes pleasant ethereal odour, and burn with a very smoky flame. Many, especially benzene and its methyl derivatives, occur in the lower fractions from coal-tar; others are prepared synthetically by *Fittig's* or *Friedel-Crafts'* methods.

Modes of Formation.—1. *Fittig's Synthesis.*—By treating a mixture of a brominated benzene hydrocarbon and an alkyl iodide or bromide with sodium in the presence of dry ether (A. **131**, 303):



$$C_6H_5Br + CH_3I + 2Na = C_6H_5·CH_3 + NaI + NaBr;$$
$$C_6H_4Br(C_2H_5) + C_2H_5I + 2Na = C_6H_4(C_2H_5)_2 + NaI + NaBr.$$

Formula.	Name.	Constitution Formula.	Positions of Substituents.	Melting-point.	Boiling-point.	Specific Gravity.
C_6H_6	Benzene	C_6H_6	...	5·4°	80·4°	0·874
C_7H_8	Toluene	$C_6H_5 \cdot CH_3$	...	liquid	110°	0·869
C_8H_{10}	*o*-Xylene	$C_6H_4(CH_3)_2$	1:2	−28°	142°	0·893
	m-Xylene	$C_6H_4(CH_3)_2$	1:3	−53°	139°	0·881
	p-Xylene	$C_6H_4(CH_3)_2$	1:4	+13°	138°	0·880
	Ethylbenzene	$C_6H_5 \cdot C_2H_5$	...	liquid	136°	0·883
C_9H_{12}	Hemimellithene	$C_6H_3(CH_3)_3$	1:2:3	liquid	175°	...
	Pseudo-cumene	$C_6H_3(CH_3)_3$	1:2:4	liquid	169·5°	0·895
	Mesitylene	$C_6H_3(CH_3)_3$	1:3:5	liquid	165°	0·865
	o-Methylethylbenzene	$C_6H_4(CH_3)(C_2H_5)$	1:2	liquid	159°	...
	m-Methylethylbenzene	$C_6H_4(CH_3)(C_2H_5)$	1:3	liquid	159°	...
	p-Methylethylbenzene	$C_6H_4(CH_3)(C_2H_5)$	1:4	liquid	162°	...
	n-Propylbenzene	$C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CH_3$	...	liquid	159°	0·867
	Cumene	$C_6H_5 \cdot CH(CH_3)_2$	...	liquid	153°	0·866
$C_{10}H_{14}$	Durene	$C_6H_2(CH_3)_4$	1:2:4:5	80°	192°	...
	Isodurene	$C_6H_2(CH_3)_4$	1:2:3:5	...	195°	...
	Metacymene	$CH_3 \cdot C_6H_4 \cdot CH(CH_3)_2$	1:3	...	175°	0·862
	Cymene	$CH_3 \cdot C_6H_4 \cdot CH(CH_3)_2$	1:4	...	175°	0·856

Jannasch synthesised *p*-xylene, durene, and isodurene by this method.

2. *Friedel* and *Crafts' Synthesis* (1877).—By the action of alkyl chlorides (bromides or iodides) on aromatic hydrocarbons in the presence of anhydrous aluminic chloride, ($AlCl_3$):



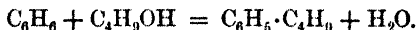
$$C_6H_6 + CH_3Cl = C_6H_5{\cdot}CH_3 + HCl;$$
$$C_6H_6 + 2CH_3Cl = C_6H_4(CH_3)_2 + 2HCl, \&c.$$

This reaction is, like the preceding one, capable of very wide application; by means of it all the hydrogen atoms in benzene can be gradually replaced by methyl. The best yields are often obtained by the addition of carbon bisulphide, which serves as a diluent, and also prevents the temperature rising to any appreciable extent, and thus largely avoids the decomposing or differentiating action of the chloride on the homologues first formed. At higher temperatures, for example, $C_6H_5{\cdot}CH_3$ would be transformed to a large extent into C_6H_6 and $C_6H_4(CH_3)_2$ (B. 1894, **27**, 1606, 3235).

Zinc, antimony, and ferric chlorides (*Nencki*, B. 1899, **32**, 2414; *Menschutkin*, Abs. 1914, i, 188, 673) act in the same way as chloride of aluminium, while ethyl chloride and other halide compounds, such as chloroform and acid chlorides, may replace methyl chloride. (See respectively triphenyl-methane and the ketones; cf. also B. **14**, 2624; **16**, 1744; Ann. de chim. et phys. [6] **1**, 419; B. **30**, 1766.) The metallic chloride forms additive compounds with the acyl chloride or alkyl derivative, *e.g.* $CH_3{\cdot}COCl$, $AlCl_3$, and also with the condensation product, *e.g.* $C_6H_5{\cdot}CO{\cdot}CH_3$, $AlCl_3$ (*Perrier*, B. 1900, **33**, 815). The reaction is a unimolecular one, except when an excess of $AlCl_3$ is used.

For further discussion, see Chap. XLIX, G.

Alcohols also, like the alkyl halides, are capable of reacting in an analogous manner in presence of $ZnCl_2$:



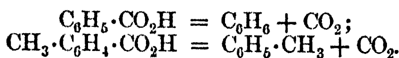
$$C_6H_6 + C_4H_9OH = C_6H_5{\cdot}C_4H_9 + H_2O.$$

3. A method of formation somewhat analogous to the *Fittig* synthesis is the action of alkyl iodides or methyl sulphate on organo-magnesium halides (*Grignard's* compounds) in toluene solution (*Houben*, B. 1903, **36**, 3083; 1904, **37**, 488; *Werner*, *ibid.*, 2116, 3618):



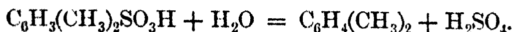
$$CH_3{\cdot}C_6H_4{\cdot}MgBr + C_2H_5Br = CH_3{\cdot}C_6H_4{\cdot}C_2H_5 + MgBr_2.$$

4. The benzene hydrocarbons are formed when their carboxylic acids are distilled with soda-lime:



$$C_6H_5{\cdot}CO_2H = C_6H_6 + CO_2;$$
$$CH_3{\cdot}C_6H_4{\cdot}CO_2H = C_6H_5{\cdot}CH_3 + CO_2.$$

5. From sulphonic acids (Chap. XXIII) by the elimination of the SO_3H group:



$$C_6H_3(CH_3)_2SO_3H + H_2O = C_6H_4(CH_3)_2 + H_2SO_4.$$

This reaction can be effected by dry distillation, by heating with concentrated hydrochloric acid to 180°, by distillation of the ammonium salt (*Caro*), or by treatment with superheated steam, *e.g.*, in presence of concentrated sulphuric acid (*Armstrong, W. Kelbe*); also by heating with concentrated phosphoric acid (B. **22**, Ref. 577).

6. From the amino-compounds by transforming these into diazonium-compounds (Chap. XXII, A), and boiling the latter with absolute alcohol or with an alkali stannite solution (B. **22**, 587). *Griess* reaction.

7. By distillation of the phenols (or ketones) with zinc dust.

Isomers and Constitution.—The table given on p. 373 shows that the benzene hydrocarbons, from C_8H_{10} on, exist in many isomeric modifications; thus, isomeric with the three xylenes we have ethyl-benzene, with the three trimethyl-benzenes the three methylethyl-benzenes and the two propyl-benzenes, with durene, isodurene, cymene, &c.

The *constitution* of these hydrocarbons follows very simply from their modes of formation. A hydrocarbon $C_{10}H_{14}$, for instance, which is obtained from benzene and methyl chloride by the *Friedel-Crafts'* reaction, can only be a tetramethyl-benzene; another of the same molecular formula $C_{10}H_{14}$, which has been prepared from bromo-benzene, butyl bromide and sodium, must be a butyl-benzene; while a third, from *p*-bromo-toluene, normal propyl iodide and sodium, must be a *p*-propyl-toluene (*p*-methyl-*n*-propyl-benzene), &c. The synthesis therefore determines the constitution.

The groups CH_3, C_2H_5, &c., which replace hydrogen in benzene, are termed "side chains".

When oxidized, the hydrocarbons yield a benzene-mono-, di-, or tri-, &c., carboxylic acid, *e.g.* benzoic acid, $C_6H_5{\cdot}CO_2H$, *o*-, *m*-, *p*-phthalic acid, $C_6H_4(CO_2H)_2$, according to the number of side chains present in the hydrocarbon; and a further proof of the constitution of the compound is thus afforded.

If, for example, a hydrocarbon C_9H_{12} yields a benzene-tricarboxylic acid, $C_6H_3(CO_2H)_3$, upon oxidation, it must contain three side chains, *i.e.* must be a trimethyl-benzene; should a phthalic acid, on the other hand, result, then it can only be an ethyl-toluene. Since cymene yields *p*- (or tere-) phthalic acid, $C_6H_4(CO_2H)_2$, on oxidation, its two side chains must be in *p*-positions to one another.

The respective isomers resemble each other closely in physical properties, their boiling-points, for example, lying very near together. The ortho-derivatives often boil at about 5°, and the meta- at about 1° higher than the para-compounds; the boiling-point rises with an increasing number of methyl groups. (Cf. B. 19, 2513.)

Behaviour.—1. The benzene hydrocarbons are, as a rule, readily nitrated and sulphonated, mono-, di-, and even tri-derivatives being all usually capable of preparation, according to the conditions. As a rule, it is only the hydrogen atoms of the benzene nucleus which are replaced, the side chains reacting as paraffin residues. Hexamethyl-benzene can thus neither be nitrated nor sulphonated. Exceptions to this generalization are met with, *e.g.* mesitylene yields a nitro-derivative, $C_6H_3(CH_3)_2 \cdot CH_2 \cdot NO_2$, cf. also Phenylnitro-methane, Chap. XX.

2. *Oxidation.*—Benzene itself is not readily oxidized; permanganate of potash converts it slowly into formic and oxalic acids, some benzoic acid and phthalic acid being produced at the same time. These doubtless result from some previously formed diphenyl.

The homologues of benzene, on the other hand, are readily oxidized to carboxylic acids, the benzene nucleus remaining unaltered, and each side chain—no matter how many carbon atoms it may contain—yielding, as a rule, a carboxyl group.

Nitric acid allows of a successive and often a partial oxidation of individual side chains, chromic acid mixture ($K_2Cr_2O_7 + H_2SO_4$) acts more energetically, converting all the side chains in the *p*- and *m*-compounds into carboxyl, and completely destroying the *o*-compounds. The latter may be oxidized to the corresponding carboxylic acids by $KMnO_4$.

When a hydrocarbon is selectively oxidized, the longest side chain, as a rule, is most readily oxidized; thus $C_3H_7 \cdot C_6H_4 \cdot CH_3$ yields first $CO_2H \cdot C_6H_4 \cdot CH_3$, and then $C_6H_4(CO_2H)_2$.

3. *Reduction.*—The benzene hydrocarbons and most of their derivatives are capable of taking up six atoms of hydrogen.

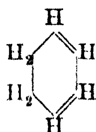
Benzene itself is only converted into hexahydro-benzene, C_6H_{12}, with difficulty, but toluene, xylene, and mesitylene combine with hydrogen more easily when they are heated with phosphonium iodide, PH_4I, at a rather high temperature, the compounds $C_7H_8 \cdot H_2$, $C_8H_{10} \cdot H_4$, and $C_9H_{12} \cdot H_6$ being formed. The two former can then be made to take up more hydrogen by energetic reaction.

An interesting method of formation of C_6H_{12} is by the action of freshly reduced nickel on a mixture of hydrogen and benzene or its homologues at moderate temperatures.

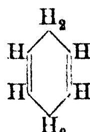
Hexahydro-benzene and its analogues, C_nH_{2n}, are colourless liquids insoluble in water, and of somewhat lower boiling-point than their mother compounds, into which they can be readily retransformed by oxidation, either by heating with sulphur or by means of fuming nitric acid, nitration also taking place in the latter case; *e.g.* hexahydro-benzene yields nitro-derivatives of benzene. They are found in petroleum, especially in that from the Caucasus (*Beilstein*, *Kurbatow*), and differ from the isomeric olefines by being insoluble in sulphuric acid, and by not forming additive products with bromine (cf. B. **20**, 1850; A. **234**, 89; **301**, 154).

They are identical with hexamethylene and its derivatives, and react as saturated compounds. The partially reduced benzene derivatives, on the other hand, behave more like olefines.

The **dihydro-benzenes**, C_6H_8, readily combine with two or four atoms of bromine, and are readily oxidized by alkaline permanganate, as might be inferred from the presence of double bonds in the molecule. Two isomeric compounds, Δ 1:3-dihydro-benzene and Δ 1:4-dihydro-benzene, are known:



Cyclohexa-1:3-diene



Cyclohexa-1:4-diene

Tetrahydro-benzene, (H, H_2, H, H_2, H_2, H_2 ring), which exists in one form

Cyclohexene

only, is readily oxidized, combines with two atoms of chlorine and bromine or with a molecule of hypochlorous acid. All are colourless, volatile liquids.

4. *Behaviour with Halogens.*—Chlorine and bromine react differently, according to the conditions. In direct sunlight they yield with benzene the additive products $C_6H_6Cl_6$ and $C_6H_6Br_6$, while in diffused daylight, especially in presence of a little iodine, $SbCl_3$ or $MoCl_5$, they give rise to the substitution products C_6H_5Cl, C_6H_5Br, &c. (For further details, and for substitution by iodine, see pp. 60 and 384).

5. Chromium oxychloride, CrO_2Cl_2, converts the methylated benzene hydrocarbons into aromatic aldehydes (Chap. XXV, B; cf. B. **23**, 1070). (*Etard's* reaction.)

6. The numerous "condensations" which benzene, &c., can undergo with oxygenated compounds in presence of $ZnCl_2$, P_4O_{10}, or H_2SO_4, and with chlorinated compounds in presence of $AlCl_3$, are of great interest; thus benzene yields diphenylethane with aldehyde and sulphuric acid, and benzophenone with benzoic acid and phosphorus pentoxide.

7. In presence of aluminic chloride, oxygen can be introduced into benzene, yielding phenol; sulphur, yielding phenyl sulphide; ethylene, yielding ethyl-benzene; carbon dioxide, yielding benzoic acid.

Benzene, C_6H_6, was discovered by *Faraday* in 1825, and detected in coal-tar by *Hofmann* in 1845. It is obtained from the portion of coal-tar which boils at 80°–85° by fractionating or freezing. It may be prepared chemically pure by distilling a mixture of benzoic acid and lime. The ordinary benzene of commerce usually contains **thiophene**, and thus gives a characteristic deep-blue coloration when shaken with a solution of isatin in concentrated sulphuric acid; but it may be freed from the impurity by repeated shaking with small quantities of sulphuric acid, which converts the thiophene into a sulphonic acid. It burns with a luminous smoky flame, and is a good solvent for resins, fats, iodine, sulphur, phosphorus, &c. When its vapour is led through a red-hot tube, diphenyl is obtained.

C_7H_8.—**Toluene**, $C_6H_5 \cdot CH_3$. Discovered in 1837. *Formation*: by the dry distillation of balsam of Tolu and of many resins. Synthesis according to *Fittig* (see above). *Preparation*: from coal-tar, in which it is found accompanied by thio-tolene. Toluene is very similar to benzene. It boils at 110°, and is still liquid at −28°. CrO_2Cl_2 converts it into benzaldehyde, and HNO_3 or CrO_3 into benzoic acid.

C_8H_{10}.—(*a*) *o*-, *m*-, and *p*-**Dimethyl-benzenes** or **Xylenes**, $C_6H_4(CH_3)_2$.—The xylene of coal-tar consists of a mixture of the three isomers, *m*-xylene being present to the extent of 70 to 85 per cent. These cannot be separated from one another by fractional distillation. *m*-Xylene is more slowly oxidized by dilute nitric acid than its isomers, and can thus be obtained with relative ease.

For the separation of these isomers by means of H_2SO_4 see B. **10**, 1010; **14**, 2625; **17**, 444; **25**, Ref. 315; and for their recognition see B. **19**, 2513. Benzene and toluene yield chiefly ortho-, together with a little para-xylene, when subjected to the *Friedel-Crafts* synthesis (B. **14**, 2627).

1. *o*-**Xylene**, which can be prepared synthetically from *o*-bromo-toluene, methyl iodide, and sodium, is oxidized to carbonic acid by chromic acid mixture, and to *o*-toluic acid, $C_6H_4(CH_3)CO_2H$, by dilute nitric acid; it is difficult to nitrate.

2. *m*-**Xylene** or **iso-xylene** can also be prepared from mesitylene, $C_6H_3(CH_3)_3$, [1:3:5], by oxidation to mesitylenic acid, $C_6H_3(CH_3)_2CO_2H$, and subsequent distillation with lime. Dilute nitric acid only oxidizes it at a temperature of 120°, while chromic acid mixture converts it into isophthalic acid, $C_6H_4(CO_2H)_2$. It yields **tetra-** and **hexahydro**-derivatives, C_8H_{14} and C_8H_{16}; the latter is present in Caucasian petroleum, and boils at 119°.

3. *p*-**Xylene** is prepared from *p*-bromo-toluene, or better, *p*-dibromo-benzene, methyl iodide, and sodium (B. **10**, 1356; B. **17**, 444). M.-pt. 13°. Dilute nitric acid oxidizes it to *p*-toluic acid, $C_6H_4(CH_3)CO_2H$, and terephthalic acid, $C_6H_4(CO_2H)_2$.

Dihydro-*p*-xylene can be prepared from ethyl succinylo-succinate. Liquid; b.-pt. 133°. It has an odour of turpentine, and is closely related to the terpenes. (Cf. *Baeyer*, B. **25**, 2122.)

(*b*) **Ethyl-benzene**, $C_6H_5{\cdot}C_2H_5$, is obtained from C_6H_5Br and C_2H_5Br by the *Fittig* reaction; from cinnamene, C_6H_5 $CH{:}CH_2$, on reduction with HI; and from C_6H_6 and C_2H_5Cl by the *Friedel-Crafts* reaction. It is found in small quantity in the xylene from tar, and when oxidized yields benzoic acid.

C_9H_{12}.—(*a*) **Trimethyl-benzenes**.—1. **Mesitylene**, 1:3:5-*tri-methyl-benzene*, $C_6H_3(CH_3)_3$.—This is contained in coal-tar along with the two other isomeric trimethyl-benzenes ("tar-cumene"), and can be synthesised from acetone or allylene. It is a liquid of agreeable odour. Nitric acid oxidizes the

side chains one by one, while chromic acid mixture decomposes it completely. (For *constitution*, see p. 364.)

2. **Pseudo-cumene**, 1:2:4-*trimethyl-benzene*, is separated from mesitylene, not by fractional distillation, but by taking advantage of the sparing solubility of pseudo-cumene-sulphonic acid (B. **9**, 258). Its constitution follows from its formation from bromo-*p*-xylene [1:4:2], and also from bromo-*m*-xylene [1:3:4], by the *Fittig* reaction. Nitric acid oxidizes the side chains successively.

3. **Hemellithene**, 1:2:3-*trimethyl-benzene* (see B. **15**, 1853), is present in coal-tar (B. **20**, 903).

(*b*) **Propyl-benzenes.**—1. *n*-**Propyl-benzene**, $C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CH_3$, is obtained from bromo-benzene and normal propyl iodide by the *Fittig* reaction, and also from benzyl chloride, $C_6H_5 \cdot CH_2Cl$, and zinc ethyl.

2. **Isopropyl-benzene** or **Cumene**, $C_6H_5 \cdot CH(CH_3)_2$, is produced by the distillation of cumic acid, $C_6H_4(C_3H_7)(CO_2H)$, with lime; from benzene and iso- or normal propyl iodide by means of $AlCl_3$, in the latter case with molecular rearrangement (p. 138); and from benzylidene chloride, $C_6H_5 \cdot CHCl_2$, and zinc methyl, this last method furnishing proof of its constitution. On oxidation, both compounds yield benzoic acid.

$C_{10}H_{14}$.—(*a*) **Durene**, 1:2:4:5- or *s-tetramethyl-benzene*, $C_6H_2(CH_3)_4$, has been found in coal-tar, and can be prepared from toluene and methyl chloride by the *Friedel-Crafts* reaction, or from dibromo-*m*-xylene (from coal-tar xylene), methyl iodide, and sodium (A. **216**, 200). It is a solid, and possesses a camphor-like odour. (For its *constitution* see B. **11**, 31.)

(*b*) **Methyl-propyl-benzenes**, $C_6H_4(CH_3)C_3H_7$.—The most important of these is **cymene** or **isopropyl-*p*-methyl-benzene.** It is found in Roman cummin oil (*Cuminum cyminum*), in eucalyptus oil, &c., and is formed when camphor is heated with P_2S_5, or better, P_4O_{10}, also when oil of turpentine is heated with iodine, &c. It has been synthetically prepared from *p*-bromo-isopropyl-benzene, methyl iodide, and sodium, and also from *p*-bromo-toluene, *n*-propyl iodide, and sodium, the *n*-propyl- changing here into the isopropyl group. It is a liquid of agreeable odour.

Cymene was formerly regarded as *normal*-propyl-*p*-methyl-benzene, but its synthesis from *p*-brom-*iso*-propyl-benzene, methyl iodide, and sodium established its constitution as an *iso*propyl derivative (cf. *Widman*, B. **24**, 439). When oxidized, it yields either *p*-toluic acid, terephthalic acid, cumic

acid, or *p*-tolyl-methyl-ketone, according to the conditions.

$C_{12}H_{18}$.—**Hexamethyl-benzene,** *Mellitene,* from methyl alcohol, acetone, and Al_2O_3, at 400°, crystallizes in prisms or plates which melt at 164°. It can neither be sulphonated nor nitrated. $KMnO_4$ oxidizes it to mellitic acid, $C_6(CO_2H)_6$.

Compounds derived from the hydrocarbon, C_7H_8, isomeric with toluene but with a semi-cyclic olefine linking have been studied by *Auwers* (B. 1911, 1595; A. 1921, **425**, 217), *e.g.* $Me_2\langle\rangle = CH_2$. These are more volatile and have lower densities than the isomeric true benzenes, into which they readily pass in the presence of acids. They also readily polymerise and are termed **semi-benzene** derivatives.

B. Unsaturated Benzene Hydrocarbons

The benzene hydrocarbons containing less hydrogen comport themselves, on the one hand, like benzene itself, and on the other like the unsaturated hydrocarbons of the fatty series, combining readily with hydrogen, halogen, halogen hydride, &c. They are derived from the olefines or acetylenes by the exchange of H for C_6H_5, thus: $C_6H_5 \cdot CH:CH_2$, cinnamene, styrene, or phenyl-ethylene; $C_6H_5 \cdot C⋮CH$, phenyl-acetylene. They are formed by the elimination of CO_2, from the corresponding acids, by the elimination of HBr from compounds of the type $C_6H_5 \cdot CH_2 \cdot CH_2Br$, and by the elimination of water from certain secondary and tertiary alcohols (C. R. 1901, 1182).

Cinnamene, $C_6H_5 \cdot CH:CH_2$, occurs along with other compounds in storax (*Styrax officinalis*), in the juice of the bark of *Liquidambar orientale*, and in coal-tar. It is formed when cinnamic acid is slowly distilled or heated with water to 200°.

It is also obtained when benzene vapour and ethylene are passed through a red-hot tube, or when *a*-bromo-ethyl-benzene, $C_6H_5 \cdot CH_2 \cdot CH_2Br$ (by action of bromine on ethyl-benzene), is heated. It is a liquid, has a characteristic odour, and boils at 140°. It changes on keeping into the polymeric meta-styrene, an amorphous transparent mass, and yields ethyl-benzene when heated with hydriodic acid. Addition of HBr converts it into *a*-bromo-ethyl-benzene, $C_6H_5 \cdot CH_2 \cdot CH_2Br$.

Phenyl-acetylene, $C_6H_5 \cdot C⋮CH$, produced by the elimination of CO_2 from phenyl-propiolic acid, is a fragrant liquid, b.-p. 142°, and yields white and pale-yellow explosive metallic compounds with solutions of silver and cuprous oxides. It

combines with water to aceto-phenone, $C_6H_5 \cdot CO \cdot CH_3$, when it is dissolved in sulphuric acid, and the solution is diluted with water, or when heated with water to 300°. With *Grignard* compounds, it yields $C_6H_5 \cdot C{:}C \cdot MgBr$, a reagent of use in synthesising acetylenic alcohols.

Styrene derivatives are obtained by the action of *Grignard* reagents on aromatic ketones, *e.g.* aceto-phenone gives $C_6H_5 \cdot CMe_2 \cdot OMgBr$ and then methyl-cinnamene, $C_6H_5CMe{:}CH_2$.

XIX. HALOGEN DERIVATIVES

	Cl		Br		I	
	M.-p	B.-p	M.-p.	B.-p	M.-p.	B.-p.
C_6H_5Cl	−45°	132°	−31°	157°	−30°	188°
$C_6H_4Cl_2$ *o*	liq.	179°	−1°	224°	+27°	286°
m	liq.	172°	liq.	220°	+40°	285°
p	+56°	173°	+87°	219°	+129°	285°
$CH_3 \cdot C_6H_4Cl$ *o*	−34°	159°	−26°	181°	liq.	211°
m	−48°	162°	−40°	184°	liq.	204°
p	+7·4°	162°	28°	185°	+35°	211·5°
$C_6H_5 \cdot CH_2Cl$	−48°	175°	...	198°	+24°	decomposes
C_6Cl_6	229°	326°	...	...	...	...

Benzene and its homologues can give rise to (A) additive compounds with bromine or chlorine, or (B) substituted derivatives.

A. Additive Compounds

These are of comparatively little importance, and are formed when the hydrocarbon is exposed for some time to chlorine or bromine vapour in bright sunlight.

Benzene hexachloride, $C_6H_6Cl_6$, exists in two stereo-isomeric modifications; the one melts at 157°, and the other sublimes at 310°. When warmed with alkali, they yield trichloro-benzene and HCl. The isomerism is probably due to the different arrangement of the halogen atoms on either side of the plane of the benzene ring in the two compounds. The **hexabromide** (*Matthews*, J. C. S. 1901, **79**, 43) melts at 212°.

B. Substituted Derivatives

Haloid substitution products in immense number are derived from the benzene hydrocarbons by the exchange of hydrogen for halogen. They are either colourless mobile liquids or

crystalline solids, insoluble in water but readily soluble in alcohol and ether, distil unchanged, and are distinguished by their peculiar odour and also, in part, by their irritant action upon the mucous membrane. They are heavier than water.

The substitution products of benzene and its homologues may be arranged in two distinct groups. In one the halogen is bound very firmly, far more so than in methyl chloride, ethyl iodide, &c.; it cannot be exchanged for OH (by means of AgOH), or for NH_2 (by NH_3), &c., but reacts with sodium (see the *Fittig* reaction, p. 368); A. **332**, 38; and magnesium (see below). All the substituted derivatives of benzene and many common derivatives of its homologues belong to this class.

In the second group, of which benzyl chloride is a good type, the halogen atoms enter into reaction as readily as do those of the halide substitution products of the methane series.

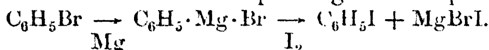
When the members of the first group are subjected to oxidation, a process which converts side chains into carboxylic groups, chloro-derivatives of benzoic and other acids are obtained. The members of the second group, when subjected to similar treatment, yield aromatic acids which are free from halogen, *e.g.* benzoic acid, $C_6H_5 \cdot CO_2H$, phthalic acid, $C_6H_4(CO_2H)_2$. From this it follows that the halogen is present in the first case in the benzene nucleus, and in the second in the side chain. Chloro-toluene is $C_6H_4Cl \cdot CH_3$, and benzyl chloride $C_6H_5 \cdot CH_2Cl$.

When the halogen atoms replace hydrogen atoms of the benzene nucleus, the products are extremely stable, and the halogen cannot readily be removed from the molecule. For exceptions, cf. B. 1892, **25**, 1495; 1895, **28**, 2312; and picryl chloride. On the other hand, when the halogen replaces hydrogen atoms of a side chain (methyl or ethyl groups), the compound is extremely reactive, and closely resembles the halogen derivatives of the fatty series. In this way it is always easy to arrive at the constitution of a compound from the behaviour of its halogen atoms and from its products of oxidation. Thus a compound $C_7H_6Cl_2$, which yields monochloro-benzoic acid upon oxidation, must be a chloro-benzyl chloride, $C_6H_4Cl \cdot CH_2Cl$.

The majority of aromatic halogen derivatives, independently of the position of the halogen in the side chain or nucleus, react in dry ethereal solution (or in benzene in presence of a little dimethyl-aniline) with dry magnesium powder, yielding organo-magnesium compounds, *e.g.* $C_6H_5 \cdot Mg \cdot Br$, phenyl-mag-

nesium bromide, $C_6H_5 \cdot CH_2 \cdot Mg \cdot Cl$, benzyl-magnesium chloride, &c. These compounds—*Grignard's* compounds—are chemically extremely active, and, like the analogous aliphatic compounds (p. 125), can be employed for the syntheses of saturated and unsaturated hydrocarbons, primary, secondary, and tertiary alcohols, thiophenols, aldehydes, ketones, acids, &c.

The *Grignard* compounds may also be used for converting a bromo-derivative into the corresponding iodo-compound, *e.g.*:



$$C_6H_5Br \underset{Mg}{\longrightarrow} C_6H_5 \cdot Mg \cdot Br \underset{I_2}{\longrightarrow} C_6H_5I + MgBrI.$$

The boiling-points of the isomeric halogen substitution products differ but little from one another (cf. *o*-, *m*-, *p*-chlorobenzene and benzyl chloride).

The influence of the introduction of F, Cl, Br, or I in place of hydrogen on the boiling-point of a hydrocarbon is similar to that noted in the fatty series. Iodine raises the boiling-point to the greatest extent, and fluorine to the least.

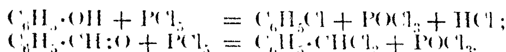
The halogen derivatives may be nitrated, sulphonated, &c., in much the same manner as benzene itself.

Modes of Formation.—1. By the action of chlorine or bromine upon aromatic hydrocarbons there are formed, according to the conditions, either additive or substitution products, the latter class especially in presence of iodine or some other halogen carrier. The function of the halogen carrier, *e.g.* I, P, Fe, &c., is probably to form an additive compound with the halogen, *e.g.* ICl_3, PCl_5, $FeCl_3$, then to give up part or the whole of the halogen in the nascent state to the hydrocarbon, and then to be immediately converted back into the above compounds again. (Cf. p. 59, also B. **18**, 607.) In many cases the rate of substitution is directly proportional to the concentration of the catalyst (*Slator*, J. C. S. 1903, 729). Iodine only substitutes directly under the conditions detailed at p. 60. From benzene most of the chlorinated derivatives up to C_6Cl_6 can be obtained in succession; the last-named compound is formed with the aid of $MoCl_5$, ICl_3, &c., at a somewhat high temperature. A hexabromo-benzene and a hexa-iodo-compound also exist. In the case of toluene and its homologues the halogen enters the benzene nucleus alone if the operation is performed in the cold, with the exclusion of direct sunlight or with the addition of iodine; while if the gas is led into the boiling hydrocarbon, or if the experiment is conducted in sunlight and without addition of iodine, it goes almost exclusively into the side chain (*Beilstein*; *Schramm*; see also B. **13**, 1216).

In the ordinary processes of substitution only half the halogen used enters the hydrocarbon molecule, the remainder is used up in forming halogen hydride. Working with bromine or iodine in the presence of concentrated nitric acid, *Datta* and *Chatterjee* (J. A. C. S. 1916, **38**, 2545; 1917, **39**, 435; 1919, **41**, 292) obtained good yields of bromo- and iodo-substitution products without the formation of halogen hydride.

The addition of $AlCl_3$ to a mixture of sulphur monochloride and sulphuryl chloride forms a powerful chlorinating agent (J. C. S. 1922, 1015).

2. From compounds containing oxygen (the phenols, aromatic alcohols, aldehydes, ketones, and acids), by the action of phosphorus pentachloride or bromide:



$$C_6H_5 \cdot OH + PCl_5 = C_6H_5Cl + POCl_3 + HCl;$$
$$C_6H_5 \cdot CH{:}O + PCl_5 = C_6H_5 \cdot CHCl_2 + POCl_3.$$

3. From the primary amines. The amine is first converted into a diazonium salt (Chap. XXII A), and this is then warmed with solutions of cuprous chloride or bromide, when the corresponding chlorine or bromine compound is obtained. If the diazonium salt is warmed with potassium iodide solution, iodo-substitution products are obtained:



$$C_6H_5 \cdot N(Cl){:}N = C_6H_5Cl + N_2;$$
$$C_6H_5 \cdot N(Cl){:}N + KI = C_6H_5I + N_2 + KCl.$$

Gattermann's modification consists in transforming the amine into the diazonium chloride, bromide, or iodide, and then decomposing this with finely-divided copper powder (*Sandmeyer*, B. **17**, 1633, 2650; *Gattermann*, B. **23**, 1218):



$$C_6H_5 \cdot NI{:}N = C_6H_5I + N_2.$$

p-**Dibromo-benzene** is obtained, together with bromo-benzene, by bromination of benzene in presence of a little iron.

The **trichloro-benzene** which results by direct substitution has the (asymmetric) constitution 1:2:4. It may also be formed by the separation of 3 HCl from $C_6H_6Cl_6$.

Hexachloro- and **hexabromo-benzenes** are produced by the prolonged chlorination or bromination of benzene, toluene, naphthalene, &c., and also from carbon tetrachloride and bromide, cf. p. 371. They are solids and can be distilled.

When toluene is chlorinated or brominated, as given on p. 384, the para- and ortho-compounds are formed in approximately equal quantities. *m*-Chloro-toluene is obtained from

chloro-*p*-toluidine, $C_6H_3Cl(NH_2)CH_3$ (from *p*-toluidine and Cl), according to method 3. Oxidation by HNO_3, CrO_3, or $KMnO_4$ converts them into the halogenated benzoic acids, but chromic acid mixture must only be used in the case of the *p*- and *m*-, and not in that of the *o*-compounds, as it completely disintegrates the latter.

Benzyl chloride, $C_6H_5{\cdot}CH_2Cl$ (*Cannizaro*), is prepared by chlorinating boiling toluene, and benzyl bromide in an analogous manner; the latter can be converted into benzyl iodide by potassium iodide solution. The behaviour of these compounds shows them to be the halide esters of benzyl alcohol, $C_6H_5{\cdot}CH_2{\cdot}OH$, from which they may be obtained by the action of halogen hydride, or of halogen derivatives of phosphorus, and into which they are transformed by prolonged boiling with water, or better, with a solution of potassium carbonate. When boiled with potassium acetate, the chloride yields benzyl acetate, with potassium sulph-hydrate the mercaptan, and with ammonia the amine.

The compounds containing halogen in the side chain irritate the mucous membrane of the nose and eyes exceedingly, and on oxidation yield benzoic acid. Benzyl chloride is used on the large scale for the preparation of oil of bitter almonds and also of certain dyes.

Benzal chloride, *Benzylidene chloride*, $C_6H_5{\cdot}CHCl_2$, and **benzo-trichloride**, $C_6H_5{\cdot}CCl_3$, are produced by the further chlorination of boiling toluene and also by the action of PCl_5 upon the corresponding oxygen compounds, benzaldehyde, $C_6H_5{\cdot}CHO$, benzoic acid, $C_6H_5{\cdot}CO_2H$, and benzoyl chloride, $C_6H_5{\cdot}COCl$. They are liquids resembling benzyl chloride, and are reconverted into the original oxygen compounds by superheating with water, and into benzoic acid by oxidizing agents.

Chlorobromo-benzenes, C_6H_4ClBr, **chlor-iodo-benzenes**, and other mixed derivatives also exist in large number.

Substitution compounds of unsaturated hydrocarbons are likewise known, *e.g.* β-**bromo-styrene**, $C_6H_5{\cdot}CBr{:}CH_2$, α-**bromo-styrene**, $C_6H_5{\cdot}CH{:}CHBr$, &c.

Iodine Derivatives containing a Polyvalent Iodine Atom.—The iodine atom attached to the nucleus may in many cases unite with other atoms, and thus exercise a higher valency. The compounds thus obtained have but few analogues in the fatty series.

Phenyl-iodide dichloride, $C_6H_5{\cdot}I{:}Cl_2$ (*Willgerodt*), is formed

as a yellow crystalline compound when dry chlorine is led into a chloroform solution of phenyl iodide. The chlorine is loosely combined, and may be removed on warming, or by the action of potassium iodide. Alkalis transform the dichloride into **iodoso-benzene,** $C_6H_5 \cdot I{:}O$, a yellow amorphous substance which dissolves in acids, yielding salts, *e.g.* **acetate,** $C_6H_5 \cdot I(C_2H_3O_2)_2$, **nitrate,** $C_6H_5 \cdot I(O \cdot NO_2)_2$, &c. It decomposes when heated, oxidizes potassium iodide solution, and when kept or when distilled in steam is converted into phenyl iodide and **iodoxy-benzene,** $C_6H_5 \cdot IO_2$. This latter is crystalline, explodes when heated, is not basic, and resembles peroxides. It may also be prepared by oxidizing the iodoso-compound with *Caro's* reagent.

Iodonium compounds (*Hartmann* and *V. Meyer*, B. **27**, 1592), *e.g.* **diphenyl-iodonium iodide,** $(C_6H_5)_2I \cdot I$, and the corresponding **hydroxide,** $(C_6H_5)_2I \cdot OH$, can be obtained when a mixture of iodoso- and iodoxy-benzene is shaken with moist silver oxide:



$$C_6H_5 \cdot I{:}O + C_6H_5 \cdot IO_2 + Ag \cdot OH = (C_6H_5)_2I \cdot OH + AgIO_3.$$

The hydroxide which is only known in solution has strongly alkaline properties. The salts, which crystallize well, closely resemble the thallium salts. It is highly probable that the three valencies of the polyvalent iodine atom in these iodonium salts lie in the same plane, as, according to *Peters* and *Kipping* (J. C. S. 1902, 1350), stereo-isomerides of the form $RR'I \cdot X$ do not appear to exist, and no resolution into optically active components can be effected.

XX. NITRO-SUBSTITUTION PRODUCTS OF THE AROMATIC HYDROCARBONS

When benzene and its derivatives are treated with concentrated nitric acid, most of them are easily dissolved, with evolution of heat, and transformed into nitro-compounds which are precipitated on the addition of water. According to the conditions of the experiment and the nature of the compound to be nitrated, one or more nitro-groups enter the molecule (see, *e.g.*, phenol). The nitro-groups substitute in the nucleus, and only very seldom in the side chain (cf. p. 391).

Very often fuming nitric acid or a mixture of fuming nitric and concentrated sulphuric (or fuming sulphuric) acid is used.

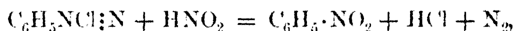
The advantage of the addition of sulphuric acid is to keep the nitric acid from becoming too dilute. The stronger the acid and the higher the temperature, the larger the number of nitro-groups introduced. The homologues of benzene are, as a rule, nitrated more readily than benzene itself.

Anhydrous pyridinium nitrate in presence of excess of pyridine is useful for nitrating the higher hydrocarbons. (*Bull. Soc.*, 1922 [IV], **31**, 91).

SUMMARY

		Positions of Substituents.	M.-p.	B.-p.	Sp. gr.
$C_6H_5{\cdot}NO_2$........	Nitro-benzene	...	+3°	208°	1·204
$C_6H_4(NO_2)_2$.......	*o*-Dinitro-benzene......	1:2	117°	319°	...
	m-Dinitro-bezene	1:3	90°	302°	...
	p-Dinitro-benzene.....	1:4	172°	299°	...
$C_6H_3(NO_2)_3$.......	*s*-Trinitro-benzene.....	1:3:5	122°	†	...
	as-Trinitro-benzene ..	1:2:4	57·5°	...	...
$CH_3{\cdot}C_6H_4{\cdot}NO_2$..	*o*-Nitro-toluene	*1:2	−10·5°	218°	1·168
	m-Nitro-toluene.......	1:3	+16°	230°	1·168
	p-Nitro-toluene........	1:4	51°	234°	1·123 (54°)
$CH_3{\cdot}C_6H_3{\cdot}(NO_2)_2$	2:4-Dinitro-toluene...	1:2:4	70°	†	...
	2:6-Dinitro-toluene...	1:2:6	66°	...	...
$(CH_3)_2{\cdot}C_6H_3{\cdot}NO_2$	4-Nitro-xylene.........	1:3:4	+2°	246°	1·135
$(CH_3)_3C_6H_2{\cdot}NO_2$..	Nitro-mesitylene......	1:3:5:2	44°	255°	...

Nitro-compounds are also produced by the action of nitrous acid upon diazonium compounds in the presence of cuprous oxide (*Sandmeyer*, B. **20**, 1494):



$$C_6H_5NCl{:}N + HNO_2 = C_6H_5{\cdot}NO_2 + HCl + N_2,$$

and also by the oxidation of primary aromatic amines:



$$C_6H_5{\cdot}NH_2 \longrightarrow C_6H_5{\cdot}NO_2$$

(*Bamberger*, B. 1893, **26**, 496). These reactions, however, are mainly of theoretical interest. They cannot, however, be prepared according to mode of formation 1 for nitro-methane (p. 97), *i.e.* by the action of $AgNO_2$ on C_6H_5Cl, &c.

The nitro-compounds are, for the most part, pale-yellow liquids which distil unchanged and volatilize with water vapour; some form colourless or pale-yellow crystals; sometimes they are also of an intense yellow or red colour. Many

* The positions of CH_3 group, or groups, are always given first.

† Most of the polynitro-compounds are not volatile, but decompose when heated.

of them explode when heated. They are heavier than water, and insoluble in it; but most of them are readily soluble in alcohol, ether, and glacial acetic acid.

The nitro-group in most aromatic nitro-compounds is bound very firmly, as in the case of the nitro methanes, and is not exchangeable for other groups. Like the latter compounds also, they are readily reduced in acid solution to the corresponding amines; in alkaline solution they are converted into azoxy-, azo-, and hydrazo-compounds (see these), and in neutral solution into hydroxylamine derivatives.

When reduced electrolytically, nitro-benzene can yield either phenyl-hydroxylamine, $C_6H_5 \cdot NH \cdot OH$, which is immediately transformed into *p*-amino-phenol, $OH \cdot C_6H_4 \cdot NH_2$ (*Gattermann*, B. 1893, **26**, 1814; 1894, **27**, 1927), or it can yield aniline. When hydrogen is passed into an alcoholic solution of nitro-benzene containing colloidal palladium, aniline is formed. (Cf. Chap. XLIV, C.)

Nitro-benzene, $C_6H_5(NO_2)$ (*Mitscherlich*, 1834), is formed when a mixture of sulphuric and the calculated quantity of nitric acid is added to benzene. It is a yellow liquid with an intense odour of oil of bitter almonds, solidifies in the cold, melts at +5°, and is used as a cheap scent for soaps and also for the manufacture of aniline.

Dinitro-benzenes, $C_6H_4(NO_2)_2$ are produced when benzene is boiled with fuming nitric acid; in this, as in all analogous cases, the two nitro groups take up the meta-position to one another, very little of the *o*- and *p*-compounds being formed, and after crystallizing from alcohol, pure *m*-dinitro-benzene is obtained in long colourless needles.

The *o*-compound crystallizes in plates and the *p*-compound in needles, both being colourless; they are prepared indirectly by eliminating NH_2 from the corresponding di-nitranilines.

When reduced, they yield first the three nitranilines, and then the phenylene-diamines (Chap. XXI, E).

o-Dinitro-benzene exchanges a nitro-group for hydroxyl when boiled with caustic soda, and for an amino-group when acted on by ammonia, yielding *o*-nitro-phenol, $C_6H_4(NO_2)(OH)$, and *o*-nitraniline, $C_6H_4(NO_2)(NH_2)$, respectively. These reactions appear to be characteristic of all compounds containing two nitro-groups in ortho-positions. The *m*-compound is oxidizable by $K_3FeC_6N_6$ to *α*- and *β*-dinitro-phenol.

***s*-Trinitro-benzene** crystallizes in colourless plates, melts at 122°, and forms additive compounds with aromatic hydro-

carbons, phenols, and especially with aromatic bases, *e.g.* aniline, naphthylamine. Most of these are well-defined crystalline compounds of red, reddish-brown, or black colour, and are readily resolved into their components by warm mineral acids (A. 1882, **215**, 344; J. C. S. 1901, 522; 1903, 1334; 1906, 583; 1910, 773). 773; 1916, 270, 1359, 1349).

Nitro-toluenes, $CH_3 \cdot C_6H_4 \cdot NO_2$.—When toluene is nitrated, the *p*- and *o*-compounds, with very little *m*-compound, are formed. The first is solid, crystallizing in large prisms, and the second liquid, the latter being used as a perfume under the name of "oil of mirbane"; both are employed in the colour industry. *m*-Nitro-toluene can be prepared indirectly from *m*-nitro-*p*-toluidine, $C_6H_3(CH_3)(NO_2)(NH_2)$, by the elimination of the amino-group (p. 411). Further nitration gives rise to:

Dinitro-toluenes, $CH_3 \cdot C_6H_3(NO_2)_2$, of the constitution $CH_3:NO_2:NO_2 = 1:2:4$ and $1:2:6$, the two nitro-groups being again in the *m*-position to one another in both cases. (Cf. previous page.)

Most of these nitro-compounds are of great technical importance, on account of the readiness with which they are reduced to amines.

Trinitro-tertiary-butyl-toluene, $C_6H(CH_3)[C(CH_3)_3](NO_2)_3$, is used as "artificial musk".

Chloro- and **Bromo-nitro-benzenes.**—When chloro- or bromobenzene is nitrated, *p*-chloro- (or bromo-) nitro-benzene is formed, together with smaller quantities of the *o*-compounds. The *m*-compounds must be prepared indirectly by replacing an amino-group in *m*-nitraniline by halogen. The *p*-derivatives have a higher melting-point than their isomers, and the *m*-compounds for the most part a higher one than the *o*-derivatives, this law frequently repeating itself in other cases also. The *p*-derivatives are usually also less soluble in alcohol. The *o*- and *p*-compounds, but not the *m*-, exchange halogen for hydroxyl when boiled with potash, and for the amino-group when heated with ammonia.

In *s*-**trinitro-chloro-benzene,** $C_6H_2(NO_2)_3Cl$, and in 1-chloro-2:4-dinitro-benzene the chlorine atoms have been rendered so readily exchangeable, that the compounds behave as alkyl chlorides, or even as acid chlorides; hence the name "picryl chloride", the chloride of picric acid (p. 441), for the former compound.

o-, *m*-, and *p*-**Nitro-cinnamenes,** $C_6H_4(NO_2)(C_2H_3)$, can be prepared by indirect methods. *a*-**Nitro-styrene,** $C_6H_5 \cdot CH:$

$CH \cdot NO_2$, which is formed by the action of nitrous acid on cinnamene, contains the nitro-group in the side chain, since it can be prepared from benzoic aldehyde and nitro-methane by means of zinc chloride, thus:—



$$C_6H_5 \cdot CHO + CH_3 \cdot NO_2 = C_6H_5 \cdot CH{:}CH \cdot NO_2 + H_2O.$$

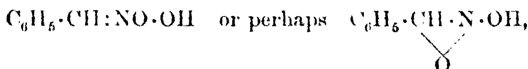
o-**Nitro-phenyl-acetylene,** $NO_2 \cdot C_6H_4 \cdot C \vdots CH$, is formed when *o*-nitro-phenyl-propiolic acid is boiled with water. It crystallizes in colourless needles.

Phenyl-nitro-methane, $C_6H_5 \cdot CH_2 \cdot NO_2$, isomeric with the nitro-toluenes, is the most typical of the aromatic nitro-derivatives with a nitro-group in the side chain. It is formed by the action of nitric acid (D 1·12) on toluene under pressure, and also by the action of benzyl halides on silver nitrite (cf. Nitro-methane). It is a true nitro-derivative, and not an alkyl nitrite (benzyl nitrite, $C_6H_5 \cdot CH_2 \cdot O \cdot N{:}O$), as it is not readily hydrolysed, and when reduced yields benzylamine, $C_6H_5 \cdot CH_2 \cdot NH_2$. It exists in two distinct modifications, which are readily transformed into each other. As generally prepared, it is a colourless liquid with a characteristic odour, boils at 225°–227°, and dissolves to a certain extent in water, yielding a solution which does not give a coloration with ferric chloride. The second modification, which is a crystalline solid melting at 84°, is formed when the sodium derivative obtained from the oily compound is decomposed in the cold by hydrochloric acid. The solid modification is relatively unstable, and when kept, gradually passes over into the oily form. The solid is probably a hydroxy-compound, since (*a*) its aqueous solution gives a red-brown coloration with ferric chloride, (*b*) it reacts with phenyl-carbimide, (*c*) it reacts with PCl_5, and (*d*) with benzoyl chloride it gives dibenzhydroxamic acid,



$$C_6H_5 \cdot CO \cdot NH \cdot O \cdot COC_6H_5 \text{ (from } C_6H_5 \cdot CH{:}N{\lt}^{O}_{O \cdot CO \cdot C_6H_5}\text{)}.$$

The solid would thus be represented by the formula:



$$C_6H_5 \cdot CH{:}NO \cdot OH \quad \text{or perhaps} \quad C_6H_5 \cdot CH \cdot N \cdot OH,$$ (with CH and N bridged by O)

an *isonitro* formula, the sodium salt by $C_6H_5 \cdot CH{:}NO \cdot ONa$, and the oil by $C_6H_5 \cdot CH_2 \cdot NO_2$. The tendency to form *iso*-nitro-compounds is also shown by certain aliphatic nitro-compounds. (Cf. Absorption Spectra, Chap. XLVII, G.)

The oily compound, although it gives rise to a sodium salt, is, strictly speaking, not an acid; it is what is termed a *pseudo-acid*, and before it yields a sodium salt it undergoes intramolecular rearrangement, yielding the true acid—the *iso*nitro-compound. When the sodium salt is treated with a mineral acid, the *iso*nitro-compound, or true acid, is first formed; but as this is unstable, it gradually changes over into the true nitro- or pseudo-acid form. Numerous examples of pseudo-acids, *i.e.* compounds which on formation of metallic salts undergo intramolecular rearrangement so that the original substance has a structure different from that of the salt, have been investigated by *Hantzsch* (B. 1899, **32**, 575; 1902, **35**, 210, 226, 1001; 1906, **39**, 139, 1073, &c.), who describes the following as some of the most characteristic criteria of pseudo-acids:—

1. The compound is a pseudo-acid if it *gradually* neutralizes an alkali. The pseudo-acid, as such, does not neutralize the base, but is first transformed into the isomeric true acid, which then neutralizes the alkali. If the transformation is slow, then the process of neutralization is also slow. Similarly, if when a solution of a salt of the acid is decomposed by an equivalent quantity of a mineral acid, the electrical conductivity gradually falls to that required for the metallic salt of the mineral acid, it indicates that the acid is a pseudo-acid, *e.g.* barium *iso*nitro-methane + HCl give isonitro-methane + $BaCl_2$, and then nitro-methane + $BaCl_2$. Isonitro-methane is a fairly strong acid, and hence is dissociated to an appreciable extent; as it becomes transformed into nitro-methane (the pseudo-acid) the conductivity will diminish, as nitro-methane is an extremely feeble acid—scarcely ionized.

2. If the original compound is extremely feebly acidic, and yet yields a sodium derivative which dissolves in water yielding a practically neutral solution, then the compound must be a pseudo-acid. It is a well-known fact that only sodium salts derived from comparatively strong acids, *e.g.* $NaCl$, Na_2SO_4, NaI, &c., dissolve in water to neutral solutions, *i.e.* are not hydrolysed by water. The sodium salts derived from feeble acids are always appreciably hydrolysed, *e.g.* Na_2CO_3, $CH_3 \cdot COONa$, &c. Hence if the sodium salt is not hydrolysed to an appreciable extent, the salt must be derived from a strong acid (the true acid), and the non- or feebly acidic compound must be the pseudo-acid.

3. If the compound in question will not yield a salt with ammonia in an anhydrous solvent, *e.g.* dry benzene, but will

do so in the presence of water, *e.g.* in moist ether, then the substance is a pseudo-acid. The formation of a salt in dry ether does not necessarily indicate that the substance is a true acid.

4. If the compound dissolves in water or in other dissociating (ionizing) media to a colourless solution, but yields a coloured solid salt or coloured ions when dissolved in alkalis, it is a pseudo-acid.

5. An abnormally high temperature coefficient for the electrical conductivity and an increase in the coefficient with rise of temperature are further indications of pseudo-acids.

Nitro-methane, bromo-nitro-methane, dibromo-nitro-methane, nitro-ethane, phenyl-nitro-methane, phenyl-bromo-nitro-methane, in addition to numerous other organic compounds, *e.g.* cyanuric acid, react as pseudo-acids.

NITROSO-DERIVATIVES OF THE HYDROCARBONS

Nitroso-benzene, $C_6H_5 \cdot N:O$, an aromatic compound which contains the nitroso-group, $\cdot N:O$, in place of a benzene hydrogen atom, is produced by the action of nitrosyl chloride, $NO \cdot Cl$, upon mercury diphenyl dissolved in benzene; it is also obtained by the oxidation of diazo-benzene with alkaline permanganate, and most readily by the oxidation of phenyl-hydroxylamine with chromic acid or ferric chloride. It forms colourless plates, melts at 68°, yields green solutions, and possesses a powerful odour similar to that of cyanic acid. When reduced it yields aniline, and when oxidized nitro-benzene. It readily condenses with different compounds, *e.g.* with aniline in the presence of acetic acid to azo-benzene:



$$C_6H_5 \cdot N:O + H_2N \cdot C_6H_5 = H_2O + C_6H_5 \cdot N:N \cdot C_6H_5,$$

and with phenyl-hydroxylamine to azoxy-benzene.

Nitroso-derivatives of tertiary amines are obtained directly by the action of nitrous acid upon the latter. (See **Nitroso-dimethyl-aniline**, $NO \cdot C_6H_4 \cdot N(CH_3)_2$, Chap. XXI, C.)

XXI. AMINO-DERIVATIVES OR ARYLAMINES*

(See Table, following page.)

Aniline, the simplest of the aromatic bases, may be regarded (1) as benzene in which a hydrogen atom is replaced by the amino-group ("amino-benzene"), or (2) as ammonia in which a hydrogen atom is replaced by phenyl, $C_6H_5\cdot$, ("phenyl-amine"). According to the former view, amino compounds can be derived from all the benzene hydrocarbons, and not only monamines (containing NH_2), but also diamines ($2NH_2$), triamines, &c.; according to the latter, the phenyl group may enter anew with the formation of secondary or tertiary amines. Secondary and tertiary amines, and even quaternary ammonium compounds, may also result from the entrance of alkyl-radicals into the above monamines, diamines, &c. Amines are also known in which the NH_2 group is attached to a carbon atom of a side chain, *e.g.* $C_6H_5\cdot CH_2\cdot NH_2$. These compounds differ in many respects from aniline and its homologues.

An extraordinarily large number of aromatic bases are thus theoretically possible, and also actually known. In certain respects they closely resemble the aliphatic amines, *e.g.* they form salts with acids, *e.g.* $C_6H_5NH_2$, HCl, and complex salts, *e.g.* platinichlorides and aurichlorides, $2C_6H_5NH_2$, H_2PtCl_6 and $C_6H_5NH_2$, $HAuCl_4$; they possess a basic odour, give rise to white clouds with volatile acids, and distil for the most part unchanged, &c. As a rule, however, they are weaker bases than the aliphatic amines, since the phenyl group, C_6H_5, possesses a negative character, and not— like the alphyl radicals— a positive; thus the salts of diphenylamine are decomposed even by water, and triphenylamine no longer possesses basic properties, while dimethyl-aniline has a strongly-marked basic character.

* To distinguish between monovalent alcoholic or hydrocarbon radicals of the fatty and aromatic series the following system has been suggested:— The term alkyl group comprises all such monovalent radicals whether of the aliphatic series, *e.g.* CH_3, C_2H_5, or of the aromatic, *e.g.* C_6H_5, $CH_3\cdot C_6H_4$, $C_6H_5\cdot CH_2$, &c. The purely aliphatic alkyl radicals are termed **alphyl groups**, and the aromatic, **aryl** (*Vorländer*, J. pr. [2], 59, 247). Thus aniline is often spoken of as a type of the arylamines.

The diamines have a more strongly basic character than the monamines, and are more readily soluble in water.

ANILINE AND ITS HOMOLOGUES

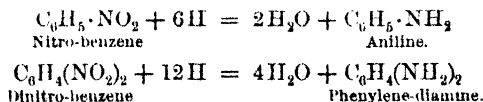
Formula.	Name.	Positions of Substituents NH_2 in 1.	M.-p.	B.-p.	M. p of Acetyl Derivative.
$C_6H_5 \cdot NH_2$.......	Aniline.............	...	−8°	183°	115°
$C_6H_4Me \cdot NH_2$...	*o*-Toluidine........	1:2	liq.	199°	110°
	m-Toluidine........	1:3	liq.	199°	65·5°
	p-Toluidine........	1:4	42·8°	198°	153°
$C_6H_3Me_2 \cdot NH_2$..	*adj.-o*-xylidene....	1:2:3	liq.	223°	134°
	unsym.-o-xylidene	1:3:4	49°	226	99°
	adj.-m-xylidene...	1:2:6	liq.	215°	176°
	p-xylidene	1:2:5	15·5°	215	139°
$C_6H_2Me_3 \cdot NH_2$..	Mesidine...........	1:2:4:6	liq.	233°	216°
	Pseudo-cumidine.	1:2:4:5	68°	234°	164°
$C_6H_5 \cdot NHMe$ ...	Methyl-aniline....	...	...	192°	101–102°
$C_6H_5 \cdot NMe_2$......	Dimethyl-aniline.	...	...	192°	...
$C_6H_5 \cdot NHEt$.....	Ethyl-aniline......	...	...	204°	54·5°
$C_6H_5 \cdot NEt_2$......	Diethyl-aniline...	...	...	213°	...
$C_6H_5 \cdot CH_2 \cdot NH_2$	Benzylamine......	...	...	183°	60°

A. Primary Monamines

Isomers.—The isomerism of the aromatic is in part analogous to that of the fatty amines (p. 110), *e.g.* dimethyl-aniline is isomeric with the methyl-toluidines and the xylidines. Cases of isomerism are also caused by the amino-group being present in the benzene nucleus in the one case, and in the side chain in the other. Finally, position isomerides are frequently met with, *e.g. o-*, *m-*, and *p*-toluidines, $CH_3 \cdot C_6H_4 \cdot NH_2$.

Constitution.—As already seen at pp. 111 *et seq.*, amines are very easy to characterize as primary, secondary, &c. In addition, their modes of formation, and also their behaviour, show whether the amino-group of a primary amine is present in the benzene nucleus or in the side chain.

Modes of Formation.—1. The most important mode of preparation of the primary arylamines, whether mono- or di-, &c., is the reduction of the corresponding nitro-compounds:



$$C_6H_5 \cdot NO_2 + 6H = 2H_2O + C_6H_5 \cdot NH_2$$
Nitro-benzene — Aniline.

$$C_6H_4(NO_2)_2 + 12H = 4H_2O + C_6H_4(NH_2)_2$$
Dinitro-benzene — Phenylene-diamine.

The usual method of introducing an amino-group into a benzene hydrocarbon is to first nitrate and then reduce. An interesting direct method for the introduction of the NH_2 group is by the action of ferric or aluminic chloride on a mixture of the hydrocarbon and hydroxylamine hydrochloride (B. 1901, **34**, 1778):



$$C_6H_6 + NH_2\cdot OH = H_2O + C_6H_5\cdot NH_2.$$

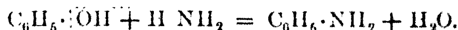
The reduction of nitro- to amino-compounds takes place most readily in acid solution, *e.g.* by the gradual addition of the former to a warm mixture of tin or stannous chloride and hydrochloric acid. On a manufacturing scale, iron and a limited amount of hydrochloric acid are used (*Béchamp*), also frequently zinc dust and hydrochloric or acetic acid. Ammonium sulphide (*Zinin*), ferrous sulphate, and baryta water, &c., also effect the reduction. (See Aniline and Chap. XLIV on Reduction.)

Aniline and its homologues may also be obtained by the electrolytic reduction of nitro-compounds.

Ammonium sulphide acts more mildly than tin and hydrochloric acid, and is therefore of special value for the partial reduction of dinitro-compounds (see Nitraniline). An alcoholic solution of stannous chloride containing hydrochloric acid may also be used for this purpose (B. **19**, 2161).

Amines are also formed when nitroso-compounds and arylhydroxylamines are reduced.

2. By heating phenols with the compound of zinc chloride and ammonia, or of calcium chloride and ammonia, to 300° (*Merz*), secondary amines being formed at the same time:



$$C_6H_5\cdot OH + H\ NH_2 = C_6H_5\cdot NH_2 + H_2O.$$

This reaction proceeds more easily in the presence of negative groups, *e.g.* with the nitro-phenols (B. **19**, 1749).

3. By distilling amino-acids with lime, sometimes by merely heating them alone:



$$NH_2\cdot C_6H_4\cdot CO_2H = C_6H_5\cdot NH_2 + CO_2.$$

4. When the hydrochlorides of secondary and tertiary amines of the type of mono- and di-methyl-aniline are heated in sealed tubes, the methyl groups wander from the nitrogen atom to a carbon atom of the benzene nucleus, *e.g.* methylaniline hydrochloride at 335° yields toluidine hydrochloride:



$$C_6H_5\cdot NHCH_3, HCl = CH_3\cdot C_6H_4\cdot NH_2, HCl.$$

The methyl groups invariably take up the *o*- or *p*-, and not the *m*- position, with respect to the amino-group.

Similarly, the final product obtained by heating phenyltrimethylammonium iodide, $C_6H_5 \cdot NMe_3I$, is mesidine hydriodide, $C_6H_2Me_3 \cdot NH_2[NH_2 : Me_3 = 1:2:4:6^*]$. Diphenylamine hydrochloride does not behave in a similar manner.

This reaction, often known as the *Hofmann* reaction, is of considerable service in obtaining the higher homologues of aniline from aniline, toluidine, &c. Aniline is readily converted into dimethyl-aniline, and when the hydrochloride of this is heated to about 300° the methyl groups wander from the side chain into the nucleus:



$$C_6H_5 \cdot NMe_2 \longrightarrow C_6H_3Me_2 \cdot NH_2.$$

5. Primary amines can be obtained from acid amides by *Hofmann's* reaction (cf. p. 191), viz. treatment with bromine and alkali, or from acid azides, $R \cdot CO \cdot N_3$. When boiled with alcohol the azide yields nitrogen and, by molecular rearrangement, a urethane, $R \cdot NH \cdot CO \cdot OEt$, and this on hydrolysis gives a primary amine, RNH_2.

6. The aromatic amines cannot, as a rule, be obtained by heating chloro-benzene, &c., with ammonia unless there is a nitro-group in the ortho- (or para-) position with respect to the halogen. Benzylamine, however, and all analogously constituted bases, which contain the NH_2 group in the side chain, can be obtained by the methods employed for the preparation of aliphatic amines. Thus benzylamine is formed by the action of ammonia, or better, of acetamide upon benzyl chloride (the latter method gives acetyl-benzylamine, which can be readily hydrolysed).

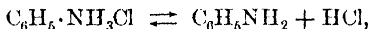
Properties.—The primary monamines are either liquid or solid crystalline bases. They are colourless when pure, but readily become brown when exposed to the air, largely owing to the presence of small amounts of impurities, and possess a weakly basic though not disagreeable odour. Aniline is somewhat soluble in water (1:31), its homologues less so.

Behaviour.—1. With acids most of them form crystalline salts, the majority of which are readily soluble in water. They do not, however, unite with very weak acids, such as

* The numbers 1:2:4:6 indicate the relative positions of the amino- and three methyl-radicals in the benzene ring.

carbonic, and they are therefore separated from their salts in the free state by sodium carbonate, and in some cases even by sodium acetate (when no acetates exist). They yield complex salts, such as **platinichlorides**, $(C_6H_5NH_2)_2, H_2PtCl_6$, **aurichlorides**, $C_6H_5NH_2, HAuCl_4$, and similar compounds with stannous, stannic, and zinc chlorides. The platinum double salts are often sparingly soluble, and therefore suited for the isolation of the bases.

All salts of the bases are readily decomposed by strong alkalis, and the free bases are regenerated. Even in aqueous solution the salts are largely split up into free acid and free base; the result is that the strength of a solution of aniline hydrochloride may be determined by titrating the hydrochloric acid present by standard alkali hydroxide, using phenolphthaleïn as indicator. This is not due to the fact that the salt is completely hydrolysed in aqueous solution; in reality there is a state of equilibrium represented by the equation:



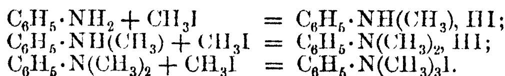
$$C_6H_5 \cdot NH_3Cl \rightleftarrows C_6H_5NH_2 + HCl,$$

and as the HCl is neutralized by the addition of alkali, more of the aniline salt is decomposed in order to restore the equilibrium. This continues until the whole of the salt is decomposed, and the HCl neutralized by the alkali.

The amines also form additive compounds with numerous metallic salts, *e.g.* $2C_6H_7N + ZnCl_2$, $2C_6H_7N + HgCl_2$, &c.

2. When aniline is heated with potassium or sodium, the hydrogen is replaced by metal with formation of the compounds C_6H_5NHK and $C_6H_5NK_2$. These yield di- and tri-phenylamine with bromobenzene, and decompose immediately with water.

3. The primary arylamines react with methyl iodide, benzyl chloride, &c., yielding secondary, tertiary, and even quaternary compounds:



$$C_6H_5 \cdot NH_2 + CH_3I = C_6H_5 \cdot NH(CH_3), HI;$$
$$C_6H_5 \cdot NH(CH_3) + CH_3I = C_6H_5 \cdot N(CH_3)_2, HI;$$
$$C_6H_5 \cdot N(CH_3)_2 + CH_3I = C_6H_5 \cdot N(CH_3)_3I.$$

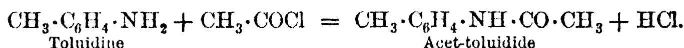
The secondary and tertiary bases can be liberated from their hydriodides by soda, but moist oxide of silver must be used in the case of the ammonium bases (see p. 112).

4. Just as the ammonium salts of acids can eliminate water, yielding amides, so the aniline salts can yield **anilides**, *e.g* aniline acetate gives acetanilide:



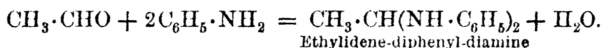
$$CH_3 \cdot CO \cdot ONH_3C_6H_5 = CH_3 \cdot CO \cdot NHC_6H_5 + H_2O.$$

These anilides may be looked upon either as acetylated amines or as phenylated amides, the formula $CH_3 \cdot CO \cdot NH \cdot C_6H_5$ corresponding with the latter view. They are in every respect analogous in their chemical behaviour to the ordinary amides, especially to the alkylated amides (p. 189). being hydrolysed to the acid and aniline by alkalis, and being formed by analogous methods, *e.g.* by heating the acid, or better, its anhydride or chloride, with the amine in question, thus:—



$$\underset{\text{Toluidine}}{CH_3 \cdot C_6H_4 \cdot NH_2} + CH_3 \cdot COCl = \underset{\text{Acet-toluidide}}{CH_3 \cdot C_6H_4 \cdot NH \cdot CO \cdot CH_3} + HCl.$$

5. Aliphatic aldehydes react with the primary bases, with elimination of water, thus:—



$$CH_3 \cdot CHO + 2C_6H_5 \cdot NH_2 = \underset{\text{Ethylidene-diphenyl-diamine}}{CH_3 \cdot CH(NH \cdot C_6H_5)_2} + H_2O.$$

Aromatic aldehydes, however, react as follows:—



$$C_6H_5 \cdot CHO + NH_2 \cdot C_6H_5 = C_6H_5 \cdot CH:N \cdot C_6H_5 + H_2O.$$

In this case an additive compound appears to be first formed, $C_6H_5 \cdot CH(OH) \cdot NH \cdot C_6H_5$, and this loses water, yielding benzylidene aniline, $C_6H_5 \cdot CH:N \cdot C_6H_5$.

Condensation products of this latter kind (**Schiff's bases**) can also be obtained with the fatty aldehydes, but they polymerize readily (*v. Miller, Plochl*, B. **25**, 2020).

6. When warmed with chloroform and alcoholic potash, the primary bases, like those of the fatty series, yield **isonitriles** of stupefying odour. When they are warmed with carbon disulphide, **thio-ureas** are formed, and from the latter **isothiocyanates (mustard oils)** by treatment with phosphoric acid (cf. pp. 285 and 306).

7. Bromine and chlorine, especially in the form of sodium hypochlorite or hypobromite, react with amines, forming substituted derivatives of the type $C_6H_5 \cdot NHBr$, in which the halogen is attached to nitrogen. These compounds are extremely unstable, can only be kept at low temperatures, and the halogen atom readily passes from the side chain into the benzene nucleus, $C_6H_5 \cdot NHBr \longrightarrow C_6H_4Br \cdot NH_2$, usually into the para-position (*Chattaway* and *Orton*, J. C. S. 1899, 1046; 1900, 134, 152, 789, 797).

8. Nitrous acid converts the primary aromatic amines in acid solution into diazonium salts (Chap. XXII, A I), and in

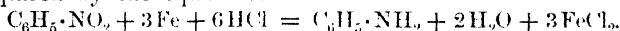
the absence of acids into diazo-amino-compounds (Chap. XXII, B). For discussion of action of nitrous acid on primary and secondary amines, see *Oddo*, G. 1914, **44**, ii, 209.

9. The oxidation products of the primary bases are very various, azo-benzene, nitro-benzene, *p*-amino-phenol, phenols, quinones, azo-compounds, aniline black, &c., resulting according to the conditions.

10. The bases which contain the amino-group in the side chain possess, in contradistinction to the purely aromatic amines, the character of the amines of the fatty series, and cannot, therefore, be diazotized.

Aniline, amino-benzene, *Phenylamine*, $C_6H_5 \cdot NH_2$, was first obtained in 1826 by *Unverdorben* from the dry distillation of indigo, and termed by him "crystalline"; then *Runge* found it in coal-tar in 1834, and called it "cyanol". In 1841 *Fritsche* prepared it by distilling indigo with potash, and gave it the name of aniline; while in 1842 *Zinin* obtained it by the reduction of nitro-benzene, and called it "benzidam". It was accurately investigated by *A. W. Hofmann* in 1843, and he was able to show that all the above products are identical.

Preparation.—Since 1864 aniline has been prepared on a manufacturing scale by reducing nitro-benzene with iron filings and a regulated quantity of hydrochloric acid, and distilling with steam after the addition of lime. The amount of hydrochloric acid actually employed is only about $\frac{1}{40}$th of that required by the equation:



$$C_6H_5 \cdot NO_2 + 3Fe + 6HCl = C_6H_5 \cdot NH_2 + 2H_2O + 3FeCl_2.$$

This is probably due to the fact that the ferrous chloride is hydrolysed to the hydroxide and free HCl; this latter then reacts with the iron and produces reduction of more nitro-benzene with formation of aniline and ferrous chloride, which is again hydrolysed, and thus the reaction becomes continuous (*Raikow*, Z. Ang. Chem. 1916, **29**, i, 196, 239). It is a colourless, oily, strongly refracting liquid of peculiar odour, which quickly turns yellow or brown in the air, and is finally converted into a resin. It dissolves in 31 parts of water, has no action upon litmus, and is a weaker base than ammonia, although it can displace the latter at higher temperatures. It is poisonous, burns with a smoky flame, and is a good solvent for many compounds which are otherwise not readily dissolved, *e.g.* indigo and sulphur. Aqueous solutions of the salts have a distinct acid reaction.

The *behaviour* of aniline has been investigated with the

utmost care. Oxidation in alkaline solution leads to azo-benzene, while arsenic acid produces chiefly violaniline, a violet colouring-matter. A solution of free aniline is temporarily coloured violet by one of bleaching-powder, this reaction being an extremely delicate one. A solution in concentrated H_2SO_4 is first coloured red and then blue by a small grain of potassium dichromate. A solution of $K_2Cr_2O_7$ produces in an acid solution of aniline sulphate a dark-green and then a black precipitate of aniline black (*Willstatter*, B. 1907, **40**, 2665; 1910, **43**, 2976; *Green*, J. C. S. 1910, 2388; B. 1911, **44**, 2570; P. 1912, **28**, 136, 250; 1913, **29**, 276; J. S. Dyers, 1913, **29**, 338), and ultimately quinone, $C_6H_4O_2$. A mixture of aniline and toluidine may be oxidized to magenta, mauveine, &c., and a mixture of aniline and *p*-diamines to safranines (see these). When reduced, aniline yields **amino-hexamethylene,** boiling at 134°.

Salts.—**Aniline hydrochloride,** $C_6H_5 \cdot NH_2$, HCl, forms large colourless plates which become greenish-grey in the air, and **aniline sulphate,** $(C_6H_7N)_2$, H_2SO_4, beautiful white plates, sparingly soluble in water. The **platini-chloride,** $(C_6H_7N)_2$, H_2PtCl_6, crystallizes in yellow plates, which are sparingly soluble.

Substitution Products—Halogen Derivatives.—Aniline is much more readily substituted by halogens than benzene, chlorine or bromine causing substitution of as many as three atoms of hydrogen, yielding *sym*-trichlor- or -tribrom-aniline, while iodine produces mono-iodoaniline. In the chlorination of aniline it is necessary to use a solvent free from water (*e.g.* chloroform or glacial acetic acid), otherwise oxidation and not substitution occurs. In bromination the simplest method is to aspirate air saturated with bromine vapour through an acid solution of aniline. In all these reactions the halogen probably first substitutes H of the NH_2 group (see p. 399). In the preparation of **monochlor-aniline,** the aniline must be "protected" by using it in the form of its acetyl derivative, acetanilide. When this is suspended in water, it is mostly transformed by chlorine into **p-chlor-acetanilide,** which readily yields ***p*-chlor-aniline** on hydrolysis; the latter forms colourless crystals, m.-pt. 71°, b.-pt. 231°. The *o*- and *m*-**compounds,** which are both liquid, are prepared indirectly, *e.g.* by the reduction of *o*- or *m*-chloro-nitro-benzene.

The basic character is weakened in the mono-chlor-anilines by the entrance of the halogen, this being the case particularly in the *o*-compounds. It is still more striking in ***s*-trichlor-**

aniline, $C_6H_2Cl_3(NH_2)$ (crystals, volatile without decomposition), which no longer combines with acids in presence of water. *o*- and *p*-Chlor-anilines are only capable of taking up two more atoms of chlorine with the formation of trichlor-aniline: [NH_2:Cl:Cl:Cl = 1.2.4.6]; *m*-chlor-aniline, on the other hand, can be further chlorinated to **tetra-** and **penta-chlor-aniline.**

The bromo-derivatives of aniline closely resemble the chlor-anilines, and may be prepared by similar methods. The best-known compound is *s*-**tribrom-aniline**, which is formed by the action of bromine water on a solution of aniline hydrochloride. It crystallizes from alcohol in needles, and melts at 119°.

As an example of the methods sometimes employed for the preparation of halogen derivatives may be cited the preparation of 2:6-dibrom-aniline from sulphanilic acid, 1-amino-benzene-4-sulphonic acid. When carefully brominated, this yields the 2:6-dibromo-derivative; and when this is superheated with steam at 170° the sulphonic acid group is removed, and **2:6-dibrom-aniline**, melting at 84°, is formed.

Nitranilines.—Aniline is likewise attacked far more violently than benzene by concentrated nitric acid, and therefore when it is wished to prepare the mono-nitro-compounds, the aniline must again be "protected", either by using its acetyl compound, or by nitrating in presence of excess of concentrated sulphuric acid. In the latter case all three nitranilines result, the *m*-compound preponderating. When acetanilide is nitrated, *p*-**nitracetanilide**, $NO_2 \cdot C_6H_4 \cdot NH \cdot CO \cdot CH_3$, and a little of the *o*-compound, are formed, and both are readily hydrolysed by potash or hydrochloric acid.

The nitranilines are further obtained by the partial reduction of the corresponding dinitro-benzenes, *e.g.* by means of ammonium sulphide; this is the method usually employed for the preparation of *m*-nitraniline. (For mechanism of the reaction, see *Cohen* and *M'Candlish*, J. C. S. 1905, 1257.)

The *o*- and *p*-compounds are also formed when *o*- and *p*-$C_6H_4Cl \cdot NO_2$, $C_6H_4Br \cdot NO_2$, $OH \cdot C_6H_4 \cdot NO_2$, or $OEt \cdot C_6H_4 \cdot NO_2$ are heated with ammonia at 180°, and conversely the *o*- and *p*-nitranilines are converted into nitro-phenols when boiled with alkalis, the former more easily than the latter, thus:—



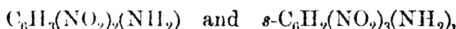
$$C_6H_4(NO_2)(NH_2) + H \cdot OH = C_6H_4(NO_2)OH + NH_3.$$

These are all further examples of the remarkable influence of nitro-groups on other substituents, *e.g.* Cl, Br, OH, NH_2,

&c., in the *o*- and *p*-, but not in the *m*-position. (Cf. Picryl Chloride, p. 444, and Picramide.)

The three nitranilines crystallize in yellow needles or prisms, and are readily soluble in alcohol, but only very slightly in water. They melt respectively at 71°, 114°, 147°, and their **acetyl** derivatives at 92°, 142°, and 207°. The *o*- and *m*-compounds are volatile with steam, but not *p*-nitraniline. When reduced, they yield phenylene-diamines.

Di- and trinitranilines,



$C_6H_3(NO_2)_2(NH_2)$ and *s*-$C_6H_2(NO_2)_3(NH_2)$,

are likewise known; the latter, which is termed **picramide**, and which crystallizes in yellow needles, m.-pt. 188°, comports itself as the amide of picric acid, since it is readily transformed into the latter compound on hydrolysis.

(For alkyl derivatives, see under Secondary and Tertiary Monamines.)

Homologues of Aniline.—Of the three **toluidines**, $CH_3 \cdot C_6H_4 \cdot NH_2$, the *o*- and *p*-compounds are obtained by the reduction of the corresponding nitro-compounds. The *o*- is liquid and the *p*- solid.

m-**Toluidine**, which is liquid, may be prepared from *m*-nitrotoluene or *m*-nitro-benzaldehyde (cf. B. **15**, 2009).

The boiling-points of the three isomeric toluidines are almost identical, but the melting-points of their acetyl compounds differ widely (see table, p. 395): these are, therefore, of value for the characterization of the toluidines. *o*-Toluidine is coloured violet by a solution of bleaching-powder, and blue by sulphuric and nitrous acids and also by ferric chloride, but not *p*-toluidine. For their conversion into fuchsine, see Triphenylmethane dyes. If during oxidation the amino group be protected by the introduction of acetyl, the methyl radical can be oxidized to carboxyl and an acetyl derivative of amino-benzoic acid obtained. When oxidized with $KMnO_4$, the amino-compounds are transformed into azo-compounds.

(For higher homologues, see table, p. 395.)

B. Secondary Monamines

We have purely aromatic secondary amines, such as **diphenylamine**, $(C_6H_5)_2NH$, and mixed secondary bases, which contain both an alphyl and an aryl group, *e.g.* **methylaniline**, $C_6H_5 \cdot NH \cdot CH_3$.

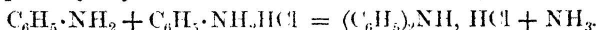
Modes of Formation.—1. Mixed secondary amines are formed when the primary amines are heated with alphyl iodides (*Hofmann*) (see p. 108), or with the alcohol and a condensing agent, *e.g.* H_2SO_4, under pressure.

This reaction does not usually stop short with the introduction of one alphyl radical, but extends further with the formation of tertiary bases. A method of separating any unaltered primary amine is by means of ethyl oxalate, which condenses with the primary but not with the secondary base, and the products can be separated by fractional distillation (*J. Thomas*, J. C. S. 1917, **111**, 562).

The secondary bases are separated from the tertiary by treatment with nitrous acid (see below, under Nitrosamines).

2. A convenient method is the reduction of the primary amine and an aldehyde in an alkaline medium, *e.g.* zinc and caustic soda. Aniline and formaldehyde yield methylaniline (*Morgan*, 1917).

3. The purely aromatic secondary amines are obtained when the primary arylamines are heated with their hydrochlorides:



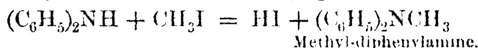
$$C_6H_5\cdot NH_2 + C_6H_5\cdot NH_2HCl = (C_6H_5)_2NH, HCl + NH_3.$$

Two different aryl radicals may be introduced, *e.g.* $(C_6H_5\cdot NH\cdot C_6H_4\cdot CH_3$, phenyl-tolylamine.

Behaviour.—1. The mixed secondary bases have strongly-marked basic properties, while the purely aromatic are feebler bases than the primary alphylamines (cf. Chap. XXI, Intr.).

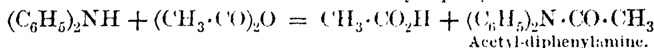
2. For the migration of the alphyl group from the side chain into the nucleus, see p. 397.

3. The hydrogen of the imino-group is replaceable by an alkyl or acyl radical, and also by potassium or sodium:



$$(C_6H_5)_2NH + CH_3I = HI + (C_6H_5)_2NCH_3$$

Methyl-diphenylamine.

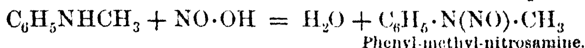


$$(C_6H_5)_2NH + (CH_3\cdot CO)_2O = CH_3\cdot CO_2H + (C_6H_5)_2N\cdot CO\cdot CH_3$$

Acetyl-diphenylamine.

4. The secondary bases give neither the isonitrile nor the "mustard oil" reaction (p. 399).

5. With nitrous acid, nitrosamines are formed (cf. p. 111):



$$C_6H_5NHCH_3 + NO\cdot OH = H_2O + C_6H_5\cdot N(NO)\cdot CH_3$$

Phenyl-methyl-nitrosamine.

These **nitrosamines** are neutral oily liquids insoluble in water, and they regenerate the secondary bases when heated with stannous chloride or with alcohol and hydrochloric acid. With mild reducing agents they yield hydrazines.

They serve for the preparation of the pure secondary bases, since they alone are precipitated by sodium nitrite as non-basic oils from the acid solution of a mixture of primary, secondary, and tertiary bases. When such nitrosamines are digested with alcoholic hydrochloric acid, a molecular re-arrangement takes place, and compounds of the nature of nitroso-dimethyl-aniline (p. 406) are formed, the nitroso-group becoming attached to a carbon atom of the nucleus (*O. Fischer* and *Hepp*, B. **19**, 2991; **20**, 1247):



$$C_6H_5\cdot N(NO)\cdot CH_3 = NO\cdot C_6H_4\cdot NHCH_3.$$

All nitrosamines give *Liebermann's* reaction (p. 438).

Methyl aniline, $C_6H_5\cdot NHMe$, is a colourless oil lighter than water. It is a stronger base than aniline; its **sulphate** does not crystallize, and is soluble in ether. For oxidation, cf. B. 1902, **35**, 703.

Diphenylamine, $NHPh_2$, crystallizes in colourless plates, melts at 54°, distils at 302°, and its solution in sulphuric acid yields an intense blue colour with a trace of nitric acid (delicate test). It is prepared by heating aniline and aniline hydrochloride at 210°–240°. The **nitrosamine**, $NPh_2\cdot NO$, forms yellow plates melting at 66·5°, and the **acetyl-derivative**, $NPh_2\cdot CO\cdot CH_3$, melts at 103°. Numerous **nitro-derivatives** are known, *e.g.* $[C_6H_2(NO_2)_3]_2NH$, which is feebly acidic in properties: its ammonium salt is the dye aurantia.

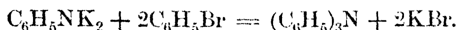
C. Tertiary Monamines

These also are either purely aromatic (triarylamines) or mixed (alphyl-arylamines).

Modes of Formation.—1. The latter are formed when the primary or secondary bases are alkylated (cf. p. 404). Methyl bromide, iodide or sulphate are often used on the small scale, but on the manufacturing scale methyl alcohol and hydrochloric acid under pressure. Primary and secondary amines can be removed by the action of ethyl chloroformate, which converts them into urethanes (p. 291), and the tertiary base then dissolved by means of dilute hydrochloric acid.

A convenient laboratory method is that due to *Noelting* (B. 1891, **24**, 563; J. C. S. 1904, **85**, 236). The primary amine is heated on the water-bath with a slight excess of the alkyl iodide and sodium carbonate solution, and in many cases an almost theoretical yield of the tertiary amine is formed. Tertiary bases are also formed when the quaternary salts are strongly heated.

2. Triphenylamine, a purely aromatic base, is formed by the action of bromobenzene upon dipotassium-aniline:

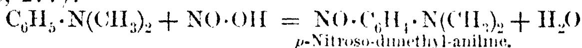


$$C_6H_5NK_2 + 2C_6H_5Br = (C_6H_5)_3N + 2KBr.$$

Behaviour.—1. Unlike the alphyl-arylamines, the purely aromatic tertiary amines are incapable of forming salts.

2. They do not yield isonitriles with $CHCl_3$, isothiocyanates with CS_2, or acyl derivatives with acid chlorides, but most of them yield quaternary compounds with methyl iodide.

3. Nitrous acid reacts with the tertiary aromatic bases, yielding coloured **nitroso-compounds** which contain the NO-group linked to the benzene nucleus; but in certain cases, *e.g.* dimethyl-*p*-toluidine, it can act as a nitrating agent (J.C.S. 1930, 277):



$$C_6H_5{\cdot}N(CH_3)_2 + NO{\cdot}OH = \underset{p\text{-Nitroso-dimethyl-aniline.}}{NO{\cdot}C_6H_4{\cdot}N(CH_3)_2} + H_2O$$

Such nitroso-derivatives can be reduced to diamines and hydrolysed to nitroso-phenols.

4. The tertiary amines, when oxidized with hydrogen peroxide, yield unstable oxides, *e.g.* **dimethyl-phenylamine oxide,** $C_6H_5{\cdot}NMe_2{:}O$, feebly basic compounds soluble in water, and decomposed at high temperatures. (Cf. Chap. XLVI, C.)

5. Tertiary amines in which the three substituents are different, *e.g.* methyl-ethyl-aniline or benzyl-phenyl hydrazine, do not exist in isomeric forms, and cannot be resolved into optically active components (*Kipping* and *Salway*, J. C. S. 1904, 438; *H. O. Jones* and *Millington*, C. C. 1904, **2**, 952). The centres of gravity of the nitrogen atom and of the three substituents would therefore appear to lie in one plane.

6. Tertiary amines containing a benzyl group are decomposed by acetic anhydride, yielding benzyl acetate and the acetyl derivative of a secondary amine.

Dimethyl-aniline, $C_6H_5{\cdot}N(CH_3)_2$, is an oil of sharp basic odour, solidifying in the cold; its salts do not crystallize well. It combines with methyl iodide, even in the cold, to the compound $N(C_6H_5)(CH_3)_3I$, phenyl-trimethyl-ammonium iodide, which breaks up into its components when distilled. With nitrous acid it yields *p*-**nitroso-dimethyl-aniline**, which crystallizes in green plates, melting at 85°; the **hydrochloride** crystallizes in yellow needles. When oxidized with permanganate the nitroso-compound yields *p*-**nitro-dimethyl-aniline** (m.-pt. 162°), when reduced *p*-**amino-dimethyl-aniline,** and when hydrolysed with alkali *p*-**nitroso-phenol** (p. 443) and **dimethyl-**

amine. (For condensations, cf. Malachite-green, Chap. XXX.) Bleaching-powder colours dimethyl-aniline only a pale-yellow. Dimethyl-aniline yields compounds of somewhat complex composition with acid chlorides, aldehyde, &c.; for example, tetramethyl-diamino-benzophenone or, finally, methyl violet with carbonyl chloride; leuco-malachite green with benzoic aldehyde, &c. Mild oxidizing agents, such as chloranil, convert it into methyl violet. **Diethyl-aniline** boils at 213°; its **nitroso-derivative** melts at 84°.

Triphenyl-amine, NPh_3, melts at 127°, and yields no salts.

D. The Quaternary Bases

correspond entirely with the quaternary bases of the fatty series. **Trimethyl-phenyl-ammonium hydroxide,** $C_6H_5 \cdot N(CH_3)_3 \cdot OH$, for instance, is a colourless, strongly alkaline, bitter substance which breaks up into dimethyl-aniline and methyl alcohol when heated. Most of the tertiary amines, however, which contain substituents in the two ortho-positions with respect to the alphylated NH_2 group, are incapable of yielding quaternary ammonium salts, *e.g.* 2 : 6 - dibromode - methylaniline, $C_6H_3Br_2 \cdot NMe_2$. (*E. Fischer*, B. 1900, **33**, 345, 1967). This is an example of steric retardation or inhibition (cf. p. 181).

The readiness with which a given quaternary salt is formed depends to a large extent on (*a*) the order in which the radicals are introduced, (*b*) the nature of the alkyl haloid used, *e.g.* chloride bromide or iodide, the last reacting most readily, (*c*) the solvent (p. 109), and (*d*) temperature (cf. *Wedekind*, A. 1901, **318**, 90; *Jones*, B. A. Rep. 1904, 179). It has been found that in the preparation of phenyl-dimethylethyl ammonium iodide a 100-per-cent yield is obtained when methylethyl-aniline is combined with methyl iodide, but only a 15-per-cent when dimethyl-aniline is combined with ethyl iodide under similar conditions.

The quaternary salts treated with sodium chloride give tertiary bases, $C_6H_5 \cdot NMe_3Cl$ gives $C_6H_5NMe_2$.

All the quaternary compounds so far mentioned have contained 4 alkyl and 1 negative radical, *e.g.* OH_1Cl, attached to nitrogen; recently compounds of the type NR_5 have been isolated by *Schlenk* (B. 1917, **50**, 274, 823), *e.g.* $NMe_4 \cdot CH_2 \cdot C_6H_5$, a red powder obtained from NMe_4Cl and $C_6H_5 \cdot CH_2Na$ and hydrolysed by water.

E. Diamines, Triamines, &c.

Polyamino-derivatives may be obtained by reducing poly-nitro-hydrocarbons or nitro-amino-compounds, *e.g.*:



$$C_6H_4(NO_2)_2 \longrightarrow C_6H_4(NH_2)_2 \text{ (phenylene-diamine).}$$

The *o*- and *p*-diamines are best obtained from the *o*- and *p*-nitro-amino-compounds. Tetramino-benzene is formed in an analogous manner by reducing dinitro-*m*-diamino-benzene.

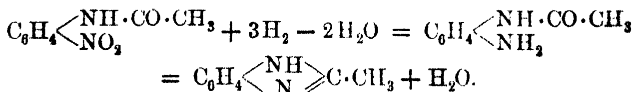
A new amino-group can be introduced in the *p*-position into an arylamine, especially a secondary or tertiary, such as $C_6H_5 \cdot N(CH_3)_2$, by first transforming the latter into an azo-dye (*e.g.* benzene-azo-dimethyl-aniline, $C_6H_5 \cdot N:N \cdot C_6H_4 \cdot NMe$) by coupling it with benzene-diazonium chloride, and decomposing this by reduction. (See the Azo-compounds.)

Diamines are also formed by the reduction of the nitroso-compounds of tertiary amines; amino-dimethyl-aniline, $NH_2 \cdot C_6H_4 \cdot N(CH_3)_2$, from *p*-nitroso-dimethyl-aniline.

The polyamines are solid compounds which crystallize in plates and distil unchanged, and are soluble in warm water. Though originally without colour, most of them quickly become brown in the air, their instability increasing with the number of amino-groups present. In accordance with the readiness with which they are oxidized, they frequently yield characteristic colorations with ferric chloride, *e.g.* *o*-phenylene-diamine a dark-red, and 1:2:3-triamino-benzene a violet and then a brown colour.

The three isomeric groups of diamines differ materially in their behaviour: (*a*) **Ortho-diamines.**—1. Ferric chloride yields a yellowish-red crystalline precipitate of diamino-phenazine hydrochloride with a solution of *o*-phenylene-diamine.

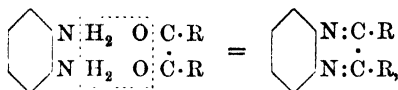
2. The mono-acyl compounds of the *o*-diamines change into derivatives of imido-azole (A. **273**, 269), the so-called "*Benz-iminazoles*" or "*Anhydro-bases*", through the formation of intramolecular anhydrides; thus *o*-nitracetanilide, when reduced with tin and hydrochloric acid, yields methyl-benziminazole or phenylene-ethenyl-amidine (A. **209**, 339):



$$C_6H_4\left\langle\begin{matrix}NH \cdot CO \cdot CH_3\\NO_2\end{matrix}\right. + 3H_2 - 2H_2O = C_6H_4\left\langle\begin{matrix}NH \cdot CO \cdot CH_3\\NH_2\end{matrix}\right.$$
$$= C_6H_4\left\langle\begin{matrix}NH\\N\end{matrix}\right\rangle C \cdot CH_3 + H_2O.$$

Compounds of this nature are also obtained by heating *o*-diamines with acids.

3. Glyoxal and many of the α-diketones yield quinoxaline and its derivatives with o-diamines:



and the α-ketonic alcohols react in an analogous manner, *e.g.* benzoïn yields dihydro-diphenyl-quinoxaline.

4. Nitrous acid converts the o-diamines into the so-called "azimino-compounds", compounds which contain three atoms of nitrogen, *e.g.* o-phenylene-diamine into azimido-benzene = imino-azo-phenylene, $C_6H_4<\overset{NH}{\underset{N}{}}\!\geqslant N$ (B. 9, 219, 1524; 15, 1878, 2195; 19, 1757).

(*b*) **Meta-diamino-bases.**—1. These form yellow-brown dyes with nitrous acid, even when only traces of the latter are present. (See Bismarck Brown, Chap. XXII, E).

2. They yield azo-dyes with benzenediazonium chloride (see Chrysoidine, Chap. XXII, E).

3. With nitroso-dimethyl-aniline, or on oxidation together with para-diamines, blue colouring-matters (indamines) are obtained, and these when boiled yield red dyes (see Toluylene red).

(*c*) **Para-diamino-compounds.**—1. When warmed with ferric chloride, or better, with $MnO_2 + H_2SO_4$, quinone, $C_6H_4O_2$ (or a homologue), is formed, and may be recognized by its odour.

2. By oxidizing para-diamines, containing one amino-group, together with a monamine or a meta-diamine, indamines are produced.

ACYL DERIVATIVES OF ARYLAMINES. ANILIDES, &c.

Practically all primary and secondary arylamines—but not tertiary—react with acids, or better, acid anhydrides or acid chlorides, yielding acyl derivatives, the most characteristic of which are the **acetyl** derivatives, *e.g.* $C_6H_5\cdot NH\cdot CO\cdot CH_3$, $CH_3\cdot C_6H_4\cdot NH\cdot CO\cdot CH_3$, $(C_6H_5)_2N\cdot CO\cdot CH_3$, &c. The acyl products formed from aniline are termed **anilides** (p. 398), *e.g.* acetanilide, benzanilide, oxanilide; they are really phenylated acid amides (see p. 189 *et seq.*), and as such may be hydrolysed, although not so readily as the amides, by means of acids or alkalis, to aniline and the corresponding acid.

The dibasic acids like oxalic acid can give rise not merely to anilides, *e.g.* $C_6H_5\cdot NH\cdot CO\cdot CO\cdot NH\cdot C_6H_5$, oxanilide, but

also to half anilides, the anilic acids, which correspond with the amic acids, *e.g.* oxanilic acid, $C_6H_5NH \cdot CO \cdot CO \cdot OH$. These are monobasic acids, and can also be hydrolysed to their components.

Similarly, the toluidines give rise to **toluidides**, *e.g.* acetoluidide, $CH_3 \cdot C_6H_4 \cdot NH \cdot CO \cdot CH_3$, and the xylidines likewise give rise to **xylidides**, &c.

The acetyl derivatives are frequently used for the identification of the various primary and secondary arylamines, since they crystallize well and have definite melting-points. As a rule, it is sufficient to mix the amine with a slight excess of acetic anhydride and warm for two minutes, and then to pour into water. After a short time the solid (or oily) acetyl derivative is obtained.

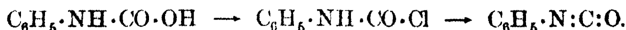
Formanilide, $C_6H_5 \cdot NH \cdot CH:O$, from aniline and formic acid, reacts as a tautomeric substance, and gives rise to two series of alkyl derivatives, one with alkyl attached to N, and the other with alkyl attached to O, the imino-ethers.

Acetanilide, $C_6H_5 \cdot NH \cdot CO \cdot CH_3$, is most conveniently prepared by boiling aniline with glacial acetic acid for twenty-four hours. It crystallizes in beautiful white prisms which are readily soluble in hot water or alcohol, less readily in ether and benzene. It melts at 115°, and boils at 304°. In the absence of water it can form a hydrochloride, C_7H_9ON, HCl. Acetanilide is used, under the name of "antifebrine", as a medicine in cases of fever.

Thio-acetanilide, $C_6H_5 \cdot NH \cdot CS \cdot CH_3$, is formed when acetanilide is heated with phosphorus pentasulphide, and from it **imido-thio-compounds, amidines**, &c., can be prepared. **Methyl-acetanilide**, $C_6H_5 \cdot N(CH_3)(C_2H_3O)$, is used as a specific against headache.

Oxanilide, $C_6H_5 \cdot NH \cdot CO \cdot CO \cdot NH \cdot C_6H_5$, is obtained when aniline oxalate is heated at 160°–180°. It melts at 252°, boils without decomposition, and is best hydrolysed by fusion with potash.

The half anilide, **oxanilic acid**, $COOH \cdot CO \cdot NH \cdot C_6H_5$, is formed when aniline oxalate is heated at 130°–140°. It melts at 149°–150°, is soluble in hot water, has the properties of a monobasic acid, and with phosphorus pentachloride yields phenyl carbimide (phenyl isocyanate):



$$C_6H_5 \cdot NH \cdot CO \cdot OH \rightarrow C_6H_5 \cdot NH \cdot CO \cdot Cl \rightarrow C_6H_5 \cdot N:C:O.$$

Diacyl derivatives of aniline and its homologues are also

known, *e.g.* $C_6H_5 \cdot N(CO \cdot CH_3)_2$, **diacetanilide.** This is formed, together with acetanilide, when aniline is boiled for an hour with excess of acetic anhydride, or when the amine is heated to a high temperature with acetyl chloride. The two may be separated by fractional distillation under diminished pressure. The diacetanilide crystallizes in colourless prisms, melts at 37°, and, unlike acetanilide, is readily soluble in benzene or light petroleum. On hydrolysis with dilute alkali, one acetyl group is split off more readily than the second.

The presence of one or two substituents in the *o*-position with respect to the amino-group of aniline facilitates the formation of diacetyl derivatives, *e.g.* *o*-toluidine yields a diacetyl derivative more readily than aniline, and *s*-tribrom-aniline yields a diacetyl derivative with the greatest readiness (J. C. S. 1901, 533).

In nearly all those compounds of the fatty series which are amino- or imino-derivatives of alcohols, acids, or hydroxy-acids, the unreplaced ammoniacal hydrogen can be substituted indirectly either wholly or partially by phenyl. The number of these phenylated (tolylated, xylylated, &c.) compounds is thus extremely large. Among them may be mentioned: **Phenyl-glycocoll,** *Phenyl-glycine,* $C_6H_5 \cdot NH \cdot CH_2 \cdot CO_2H$, from chloracetic acid and aniline; **phenyl-imino-butyric acid,** $CH_3 \cdot C(:NC_6H_5) \cdot CH_2 \cdot CO_2H$, from aniline and aceto-acetic ester; **carbanilide** or diphenyl-urea, $CO(NHC_6H_5)_2$, from aniline and carbon oxychloride (cf. p. 289); **phenyl isocyanate,** *phenyl carbimide,* $CO:N \cdot C_6H_5$, from $COCl_2$ and fused aniline hydrochloride, a sharp-smelling liquid exactly analogous to the iso-cyanic esters—its vapour gives rise to tears; **phenyl isothio-cyanate,** $C_6H_5N:CS$ (b. pt. 222°), a liquid possessing all the characteristics of the mustard oils (p. 285); **diphenyl thio-urea,** $CS(NHC_6H_5)_2$, from aniline and carbon disulphide (forms glistening plates, melting at 154°; it is decomposed into phenyl isothiocyanate and aniline when hydrolysed with concentrated hydrochloric acid.

PRIMARY AMINES WITH THE AMINO-GROUP IN THE SIDE CHAIN

These compounds resemble the primary alphylamines much more closely than aniline. As an example, we have **benzyl-amine,** $C_6H_5 \cdot CH_2 \cdot NH_2$, the amine corresponding with benzyl alcohol; it is a colourless liquid which distils unchanged. The acetyl compound, $C_6H_5 \cdot CH_2 \cdot NH \cdot CO \cdot CH_3$,

is formed by heating benzyl chloride, $C_6H_5 \cdot CH_2Cl$, with acetamide. Benzylamine is formed, together with di- and tribenzylamines, by the action of alcoholic ammonia on benzyl chloride; it is also readily obtained by reducing the phenylhydrazone of benzaldehyde:



It may also be prepared from benzyl chloride and potassium phthalimide (cf. p. 497), or from the azoimide by reduction (Abs. 1913, i, 967). Its behaviour is entirely analogous to that of methylamine, as the phenyl derivative of which it is to be regarded. It dissolves in water, and the solution thus formed is alkaline. Conductivity determinations show that it is about as strong a base as ammonia, and thus differs materially from aniline. It possesses all the characteristic properties of a primary amine, but as the NH_2 is attached to a side chain and not to the benzene nucleus it cannot be diazotized, and on treatment with nitrous acid it immediately yields benzyl alcohol.

XXII. DIAZO- AND AZO-COMPOUNDS; HYDRAZINES

A. Diazo-compounds

The primary arylamines differ characteristically from the primary alphylamines in their behaviour towards nitrous acid. The latter are converted into alcohols without the formation of intermediate products (cf. p. 111):



$$C_2H_5 \cdot NH_2 + NO \cdot OH = C_2H_5 \cdot OH + N_2 + H_2O.$$

The aromatic amines can undergo an analogous transformation; but if the temperature is kept sufficiently low, well-characterized intermediate products, the so-called **diazo-compounds** or **diazonium salts**, *e.g.* benzene-diazonium chloride, $C_6H_5 \cdot N_2Cl$, are obtained, which are of especial interest both scientifically and technically (cf. Azo-dyes, p. 417). They were discovered by *P. Griess* in 1860, and were carefully investigated by him (A. **121**, 257; **137**, 39).

The diazo-compounds are usually divided into (1) the diazonium salts, *e.g.* $\genfrac{}{}{0pt}{}{C_6H_5}{Cl}\!>\!N\!:\!N$, compounds which are analogous

to ammonium salts; (2) the true diazo-compounds, which contain the grouping ·N:N·.

I. **Diazonium Compounds.**—The diazonium salts, as a rule, are not obtained in the solid state, as they themselves are of little commercial value, but are of importance as intermediate products in various decompositions.

Solutions are usually prepared by the addition of an aqueous solution of sodium nitrite to a solution of the amine in an excess of the requisite acid (*V. Meyer*). The essentials are—(1) The solution must be kept cool, at 0° or only a few degrees above, otherwise a phenol is formed and nitrogen evolved. (2) An excess of acid must be used, otherwise diazo-amino-compounds are formed. (3) As a rule, it is advisable not to use an excess of nitrous acid. This is avoided by testing for free nitrous acid by means of potassium iodide starch paper.

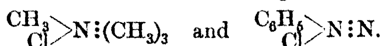
This conversion of amino- into diazo-compounds is termed "**diazotizing**".

The crystalline salts, *e.g.* benzene-diazonium chloride, may be obtained by adding concentrated hydrochloric acid to an alcoholic solution of aniline hydrochloride, and then amyl nitrite (*Knoevenagel*). They may also be obtained by the addition of alcohol and ether to their aqueous solutions.

Constitution.—The N_2X group can be attached to only one carbon atom of the benzene nucleus, since (1) when the salts undergo decomposition the products formed contain groups, *e.g.* Cl, OH, CN, &c., which are attached to a single carbon atom; (2) penta-substituted anilines, *e.g.* $SO_3H \cdot C_6Br_4 \cdot NH_2$, can be diazotized, hence *Griess'* formulæ, *e.g.* $C_6H_4N_2$, HCl, where the diazo-radical replaces two hydrogen atoms of the nucleus, are untenable.

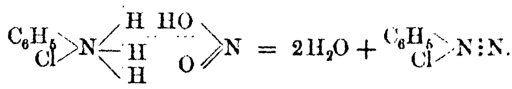
For many years the constitutional formula given to these compounds was that suggested by *Kekulé*, viz. $C_6H_5 \cdot N:N \cdot Cl$, for the chloride; this represents them as analogous to the azo-compounds. This formula readily explains the reduction of the diazonium salts to hydrazines, $C_6H_5NH \cdot NH_2$, and their conversion into azo-dyes, *e.g.* $C_6H_5 \cdot N:N \cdot C_6H_4OH$. Within the last few years a constitutional formula which was suggested by *Blomstrand* in 1875 has become generally accepted. This represents the molecule of a diazonium salt as containing a quinquevalent nitrogen atom, *e.g.* $\genfrac{}{}{0pt}{}{C_6H_5}{Cl}\!>\!N:N$. The chief arguments in favour of the *Blomstrand* formula are briefly:

1. It indicates the resemblance between the diazonium and ammonium salts, as both thus contain quinquevalent nitrogen:

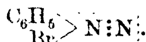


The resemblance between the two groups of compounds is marked. The diazonium salts are colourless crystalline compounds readily soluble in water; those derived from strong acids, *e.g.* the chlorides, nitrates, and sulphates, are neutral in solution, cf. NH_4Cl; whereas those derived from feeble acids, *e.g.* carbonic acid, are partially hydrolysed in aqueous solution, and hence give an alkaline reaction, cf. Na_2CO_3 or $(NH_4)_2CO_3$. In addition they form sparingly soluble platinichlorides, $(C_6H_5N_2)_2PtCl_6$, and aurichlorides, $C_6H_5N_2AuCl_4$, comparable with the ammonium compounds. The aqueous solutions of the salts are ionized to much the same extent as the corresponding quaternary ammonium salts. This resemblance of the diazonium ions to the quaternary ammonium ions is further established by a comparison of migration values. The free base, benzene-diazonium hydroxide, corresponding with ammonium hydroxide, is obtained by the action of moist silver oxide on the chloride; it dissolves readily in water, yielding strongly alkaline solutions, but is very unstable, and gradually decomposes. When neutralized with acids, it yields the above-mentioned diazonium salts.

2. The conversion of aniline and its homologues into diazonium salts is rendered somewhat more simple by such a formula:



3. The elimination of nitrogen and the formation of mono-substituted compounds, *e.g.* $C_6H_5 \cdot OH$, C_6H_5Br, &c., is readily explicable:



Cain (J. C. S. 1907, **91**, 1049) has suggested a new constitutional formula for diazonium salts, *e.g.* benzene-diazonium chloride,

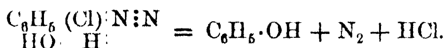


It is claimed that the double linkage between nitrogen and a

carbon atom of the benzene nucleus is more in harmony with the readiness with which the nitrogen is eliminated from the molecule. It also accounts for the fact that in a *p*-diamine only one amino-group can be diazotized.

Reactions.—1. The reaction characteristic of the diazonium salts is the readiness with which nitrogen is eliminated and monovalent groups introduced into the molecule in place of the N_2X radical, and for this reason the diazonium compounds are frequently made use of in the laboratory for the preparation of various substituted benzene derivatives. As examples of this type of reaction, we have—

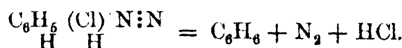
(*a*) *Replacement of* N_2X *by* OH.—An aqueous solution of a diazonium salt, especially one containing sulphuric acid, evolves all its nitrogen in the form of gas when warmed, and a phenol is formed:



This reaction, which is of very universal application, therefore allows of the exchange of NH_2 for OH. The only exceptions appear to be those salts containing numerous negative substituents in the benzene nucleus, *e.g.* $C_6H_2Br_3 \cdot N_2Cl$.

For the effect of light on the decomposition of solutions of diazonium salts, see *Orton*, *Coates*, and *Burdett*, P. 1905, 168.

(*b*) *Replacement by* H.—When diazonium-compounds, either in the solid state or dissolved in concentrated sulphuric acid, are heated to boiling with absolute alcohol, the diazo-group is generally replaced by hydrogen. In this reaction the alcohol gives up two hydrogen atoms, and is oxidized to aldehyde:



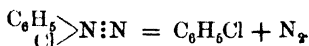
This affords a simple method for the replacement of NH_2 by H.

Instead of this reaction, there occurs in many cases an exchange of the diazo-group for the ethoxy-radical, $O \cdot C_2H_5$, with the formation of ethyl ethers of phenols; thus from chlorinated toluidines ethyl ethers of chloro-cresols are formed, and not chloro-toluenes (B. **17**, 2703; **22**, Ref. 658; **34**, 3337).

Under certain conditions stannous chloride in alkaline solution acts in an analogous manner (B. **22**, Ref. 741), while under others it gives rise to hydrazines (p. 426). In like

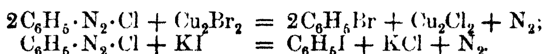
manner NH_2 may be replaced by H, by first converting an amino-compound into a hydrazine, and then decomposing the latter with $CuSO_4$ (*Baeyer*, B. **18**, 89).

(*c*) *Replacement by Halogen—Sandmeyer's Reaction.*—When a diazonium-compound is warmed with a concentrated solution of cuprous chloride in hydrochloric acid, the diazo-group is replaced by chlorine (*Sandmeyer*, B. **17**, 1633; **23**, 1218, 1628; A. **272**, 143). The same reaction takes place on distilling the diazonium platinichloride with soda, and sometimes on simply treating the diazo-compound itself with fuming hydrochloric acid, or with hydrochloric acid in presence of copper dust (*Gattermann*):



$$\begin{matrix}C_6H_5\\Cl\end{matrix}\!\!>N{:}N = C_6H_5Cl + N_2.$$

Warming with cuprous bromide yields, in the same way, a bromo-derivative (*Sandmeyer*, B. **18**, 1482), and treatment with hydriodic acid or potassium iodide an iodo-compound:



$$2C_6H_5\cdot N_2\cdot Cl + Cu_2Br_2 = 2C_6H_5Br + Cu_2Cl_2 + N_2;$$
$$C_6H_5\cdot N_2\cdot Cl + KI = C_6H_5I + KCl + N_2.$$

The amino-group may further be exchanged for bromine by boiling the diazonium perbromides (see Benzene-diazonium perbromide) with absolute alcohol.

(*d*) *Replacement by* ·CN.—This is accomplished by adding the diazotized solution to a warm solution of potassium cuprous cyanide:



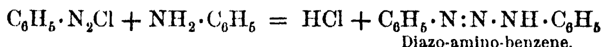
$$C_6H_5\cdot N_2Cl \rightarrow C_6H_5N_2CN \rightarrow C_6H_5\cdot CN.$$

This reaction is of importance, as the product obtained is a nitrile, and can be hydrolysed to an acid.

(*e*) Phenyl sulphide is formed by the action of hydrogen sulphide on benzene-diazonium chloride (cf. B. **15**, 1683); nitro-benzene is formed by the action of nitrous acid in presence of cuprous oxide; benzenesulphonic acid from sulphurous acid; phenyl thiocyanate from thiocyanic acid; and phenyl cyanate from cyanic acid, &c. (cf B. **23**, 738, 1218, 1454, 1628; **25**, 1086; **26**, 1996).

(*f*) When oxidized in alkaline solution, benzene-diazonium hydroxide yields—together with other products—nitroso-benzene (p. 393), and much **benzene-diazoic acid**, $C_6H_5\cdot N\cdot NO\cdot OH$, or its isomeride, **phenyl-nitramine**, $C_6H_5\cdot NH\cdot NO_2$ (m.-pt. 46°; explodes at 98°) (see B. **26**, 471; **27**, 584, 915).

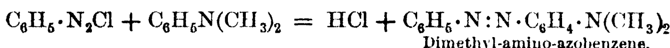
2. When a solution of a diazonium compound reacts with a primary or secondary amine, or when nitrous acid acts upon such an amine in the absence of free mineral acid, diazo-amino-compounds are formed, and these readily change into amino-azo-compounds:



$$C_6H_5 \cdot N_2Cl + NH_2 \cdot C_6H_5 = HCl + C_6H_5 \cdot N{:}N \cdot NH \cdot C_6H_5$$

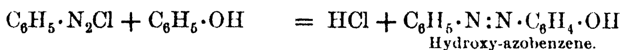
Diazo-amino-benzene.

3. **Azo-dyes.**—The diazonium salts readily react with tertiary amines or with phenols, yielding derivatives of azobenzene, *e.g.*:



$$C_6H_5 \cdot N_2Cl + C_6H_5N(CH_3)_2 = HCl + C_6H_5 \cdot N{:}N \cdot C_6H_4 \cdot N(CH_3)_2$$

Dimethyl-amino-azobenzene.



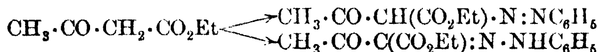
$$C_6H_5 \cdot N_2Cl + C_6H_5 \cdot OH = HCl + C_6H_5 \cdot N{:}N \cdot C_6H_4 \cdot OH$$

Hydroxy-azobenzene.

Such derivatives possess basic or acidic properties, are usually coloured yellow, red, or brown, and are known as azo-dyes.

The formation of such an azo-dye is largely made use of as a test for a primary aromatic amine with the NH_2 in the nucleus. The amine is dissolved in acid, diazotized, and then mixed with an alkaline solution of a phenol (preferably β-naphthol), when an orange-red dye is precipitated. The process is commonly spoken of as the "coupling" up of a diazonium salt with an amine or a phenol. Phenolic ethers also couple with diazonium salts (*Meyer* and *Wertheimer*, A. 1913, **398**, 66; B. 1914, **47**, 1741; *Auwers* and *Michaelis*, *ibid.*, 1275.

4. The diazonium salts react in alkaline solution with compounds containing the grouping $\cdot CH_2 \cdot CO \cdot$, yielding azo-compounds or phenylhydrazones, *e.g.*:

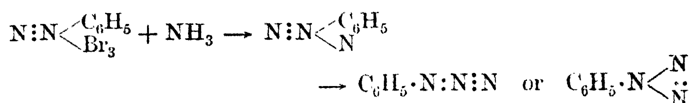


$$CH_3 \cdot CO \cdot CH_2 \cdot CO_2Et \begin{cases} \rightarrow CH_3 \cdot CO \cdot CH(CO_2Et) \cdot N{:}NC_6H_5 \\ \rightarrow CH_3 \cdot CO \cdot C(CO_2Et){:}N \cdot NHC_6H_5 \end{cases}$$

Cf. B. 1888, **21**, 1697. For the azo or hydrazone constitution of such compounds, compare *Auwers* (Abstr. 1908, i, 477; 1911, i, 168, 585).

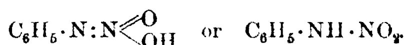
Benzene-diazonium perbromide, $C_6H_5 \cdot N_2Br, Br_2$, is a dark-brown oil, solidifying to yellow crystalline plates, and is prepared by the addition of HBr or KBr and bromine water to diazonium salts. Two of its atoms of bromine are only loosely linked. Ammonia converts it into benzene-diazo-imide, which

is to be regarded as the phenyl derivative of hydrazoic acid:



In accordance with this, dinitro-benzene-diazo-imide (from dinitro-aniline) is decomposed by alcoholic potash into dinitro-phenol and *hydrazoic acid*—a method of obtaining this latter substance by means of organic compounds (see p. 308).

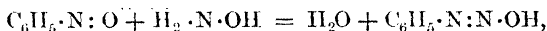
II. **Diazo-compounds.**—These contain the grouping R·N: N·X, where R = an aryl radical and X an acid radical or OH or OK. When a benzene-diazonium salt is mixed with an excess of alkali, a potassium salt, **normal potassium diazo-benzene oxide,** $C_6H_5N_2OK$, is precipitated. It crystallizes in white plates, and can be quantitatively converted into benzene-diazonium chloride; it yields ethers, and on oxidation gives nitroso-benzene and benzene-diazoic acid:



The acid, $C_6H_5N_2OH$, which corresponds with the potassium salt, is not known in a pure form. When the normal potassium salt is heated with concentrated potash at 130°–135°, it is transformed into **potassium isodiazo-benzene oxide** (*Schraube* and *Schmidt*, B. 1894, 27, 520). When this is acidified with acetic acid, the free **hydroxide** is obtained as a colourless oil which is very unstable.

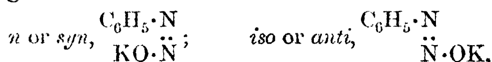
Similar *normal* and *iso*potassium derivatives have been obtained from other diazonium salts, and it has been found that the presence of negative radicals (Br, NO_2) facilitates the formation of the iso-compound,—in fact to such an extent that certain diazonium salts, when added to an alkali, immediately yield the isodiazo-compounds. Considerable controversy has taken place regarding the constitutional formulæ of these two groups of compounds. At one time the isodiazo-oxides were regarded as derivatives of phenyl-nitrosamine, viz. C_6H_5·NK·NO, and the normal compounds as true diazo-oxides, C_6H_5·N:N·OK. The researches of *Hantzsch* have proved that the two compounds are very similar as regards chemical properties. For example, both "couple" with alkaline solutions of phenols, yielding azo-dyes (p. 428), but as a rule the normal more readily than the iso-compounds. Both compounds, on reduc-

tion with sodium amalgam in the presence of a large excess of alkali, yield phenyl-hydrazine, and both compounds, on oxidation in alkaline solution, yield potassium benzene-diazoate, $C_6H_5 \cdot N:NO \cdot OK$. Similarly, both compounds yield the same benzoyl derivative by the *Schotten-Baumann* method. *Hantzsch* draws the conclusion that the two compounds are structurally identical and *stereo-isomeric*. As the *n*-diazo-oxide can be synthesised by the action of hydroxylamine on nitroso-benzene in alkaline solution (B. **38**, 2056):



$$C_6H_5 \cdot N:O + H_2 \cdot N \cdot OH = H_2O + C_6H_5 \cdot N:N \cdot OH,$$

it is probable that both normal and iso-compound are true diazo-derivatives, and that they are stereo-isomeric in much the same manner as the oximes (p. 145). According to *Hantzsch*, the normal compound has the *syn*- and the iso- the *anti*-configuration:



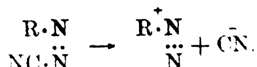
n or *syn*, $\begin{matrix} C_6H_5 \cdot N \\ KO \cdot \ddot{N} \end{matrix}$; *iso* or *anti*, $\begin{matrix} C_6H_5 \cdot N \\ \ddot{N} \cdot OK, \end{matrix}$

as the normal compounds evolve nitrogen very readily, whereas the iso-compounds are more stable. (Ber. 1894, **27**, 1702; 1895, **28**, 676, 1734; **36**, 4054; **37**, 1084.)

The isodiazo oxides or diazotates can react as tautomeric compounds, viz. as nitrosamine derivatives, $C_6H_5 \cdot NK \cdot NO$, since the potassium salt yields an N-ether, $C_6H_5 \cdot NEt \cdot NO$, whereas the silver salt yields an O-ether, $C_6H_5 \cdot N:N \cdot OEt$. *Bamberger* has suggested that the normal diazo-oxides may have a diazonium constitution $C_6H_5 \cdot N(OK) \vdots N$, whereas the iso-compound has the diazo-constitution $C_6H_5 \cdot N:N \cdot OK$; but *Hantzsch* has pointed out that the diazonium hydroxides, from which the true diazonium salts are formed, must be extremely strong bases, and could not possibly therefore possess sufficiently acidic properties to give rise to stable potassium salts which are only partially hydrolysed in aqueous solution. Certain diazo-hydroxides, $R \cdot N_2 \cdot OH$, have been isolated as colourless solids with acidic properties; the majority, however, are extremely unstable, and pass over into the isomeric nitrosamines $R \cdot NH \cdot NO$, yellow compounds with neutral properties (B. **35**, 2964; **36**, 4054; **37**, 1084). The effect of various solvents on this isomerisation has been studied by *Bamberger* and *Baudisch* (B. 1912, **45**, 2054). *p*-Nitrophenyl-nitrosamine in ether or alcohol has the diazo structure, but in chloroform the nitrosamine formula.

Corresponding with the normal and iso-diazotates, *Hantzsch* has discovered two groups of sulphonates and of cyanides, which he also regards as being stereo-isomeric in the same sense, viz. *syn* and *anti*.

In the case of *p*-anisidine, evidence of the existence of three isomeric diazo-cyanides has been obtained. The one is colourless and is an electrolyte, and hence is regarded as the diazonium salt, $OMe \cdot C_6H_4 \cdot N(CN) \vdots N$; the other two are reddish-coloured solids and non-electrolytes. The *syn*-compound is unstable, and melts at 51°; it gradually passes over into the more stable *anti*-compound, which melts at 121°. It is probable that when a *syn* diazo-cyanide is dissolved in water it is largely transformed into the ionized diazonium cyanide:



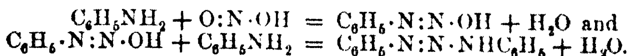
$$\begin{matrix} R \cdot N \\ NC \cdot \ddot{N} \end{matrix} \rightarrow \begin{matrix} R \cdot \overset{+}{N} \\ \vdots \\ N \end{matrix} + \overset{-}{CN}.$$

Diazonium salts, *n*-diazotates and the labile diazo-sulphonates react with sodium arsenite or a mixture of KCN and NaHS in such a manner that the N_2X group is replaced by hydrogen, whereas iso-diazotates, stable diazo-sulphonates, azo- and azoxy-compounds do not react (*Gutmann*, B. 1912, **45**, 821).

Compare also *Armstrong* and *Robertson*, J. C. S. 1905, 1280; *Hantzsch*, P. 1905, 287. For summaries see B. A. Rep. 1902, 181 (*G. T. Morgan*), and *Ahrens Sammlung*, 1902, **8**, pp. 1–82 (*Hantzsch*).

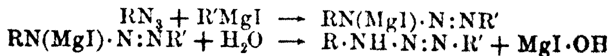
B. Diazo-amino-compounds

The diazo-amino-compounds are pale-yellow crystalline substances which are stable in the air, and do not combine with acids. They are obtained by the action of a primary or secondary amine on a diazonium salt, and also when nitrous acid reacts with a free primary aromatic amine instead of with its hydrochloride, probably:



$$C_6H_5NH_2 + O{:}N \cdot OH = C_6H_5 \cdot N{:}N \cdot OH + H_2O \text{ and}$$
$$C_6H_5 \cdot N{:}N \cdot OH + C_6H_5NH_2 = C_6H_5 \cdot N{:}N \cdot NHC_6H_5 + H_2O.$$

Diazo-amino compounds have been synthesised by the action of *Grignard* compounds on alkyl or acyl derivatives of hydrazoic acid, and decomposing the products with water:



$$RN_3 + R'MgI \rightarrow RN(MgI) \cdot N{:}NR'$$
$$RN(MgI) \cdot N{:}NR' + H_2O \rightarrow R \cdot NH \cdot N{:}N \cdot R' + MgI \cdot OH$$

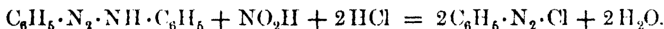
In this manner not merely aromatic but alphyl-aryl

compounds of the types $C_6H_5 \cdot NH \cdot N:N \cdot CH_3$ and $C_6H_5 \cdot CH_2 \cdot NH \cdot N:N \cdot CH_3$ have been prepared.

Reactions.—1. They are not bases, and hence do not form salts with acids.

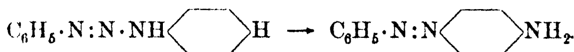
2. They behave in much the same way as the diazo-compounds, since they are usually decomposed in the first instance into their components, a diazonium salt and an amine, the former then entering into reaction. Thus diazo-amino-benzene, for example, yields phenol and aniline when boiled with water or hydrochloric acid, while with hydrobromic acid it gives bromobenzene and aniline. These reactions are easy to recognize from the accompanying evolution of nitrogen.

3. By the renewed action of nitrous acid in acid solution they are completely transformed into diazonium salts:



$$C_6H_5 \cdot N_2 \cdot NH \cdot C_6H_5 + NO_2H + 2HCl = 2C_6H_5 \cdot N_2 \cdot Cl + 2H_2O.$$

4. Most of them readily undergo molecular transformation into the isomeric amino-azo-compounds (*Kekulé*):



This molecular rearrangement takes place most readily in presence of an amine hydrochloride, which acts as a catalytic agent. The amino-group always takes up the para-position with regard to the azo-group ($\cdot N:N \cdot$) if this is free. If, however, this is already substituted, as in the diazo-amino-compound from *p*-toluidine, then the transformation occurs much more slowly, and the NH_2 takes up the *o*-position with respect to the $\cdot N:N \cdot$ group. The velocity of transformation has been investigated by *H. Goldschmidt*, and the reaction has been shown to be unimolecular. Only a relatively small amount of aniline salt is required, and the velocity is proportional to the strength of the acid, the aniline salt of which is used (B. 1896, **29**, 1899). For similar transformations, see Benzidene (p. 423) and Azoxy-benzene.

5. The imino-hydrogen of the diazo-amino-compounds is replaceable by metallic radicals, and also by acyl groups.

Constitution.—By the action of benzene-diazonium chloride upon *p*-toluidine, "diazo-benzene-*p*-toluidide" is formed, and would appear to possess the formula: $C_6H_5 \cdot N:N \cdot NH \cdot C_7H_7$ (I). But the same compound is also obtained from a mixture of *p*-toluene-diazonium chloride and aniline, a reaction which

would indicate the constitution: $C_6H_5 \cdot NH \cdot N:N \cdot C_7H_7$ **(II).**

It is all the more difficult to decide which of these two formulæ is the right one, from the fact that most of those "mixed diazo-amido-compounds" react as if they had both of the above constitutions. Thus, when the compound just mentioned is boiled with dilute sulphuric acid, it yields not only phenol and *p*-toluidine (according to I), but also aniline and *p*-cresol (according to II). Such diazo-amino-compounds are thus typical tautomeric substances. (Cf. *e.g.* B. **19**, 3239; **20**, 3004; **21**, 548, 1016, 2557; J. C. S. 1889, **55**, 412, 610, &c.)

Diazo-amino-benzene, $C_6H_5 \cdot N:N \cdot NHC_6H_5$ (*Griess*), is usually prepared by adding $NaNO_2$ (1 mol.) to the solution of aniline (2 mols.) in HCl (3 mols.), and saturating with sodium acetate (B. 1884, **17**, 641; 1886, **19**, 1952). It crystallizes in bright-yellow lustrous plates or prisms, is insoluble in water, but readily soluble in hot alcohol, ether, and benzene, melts at 98°, and is far more stable than the diazo-compounds.

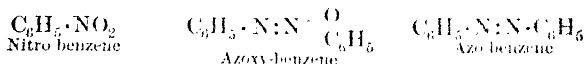
When certain *p*-diamines, *e.g.* *o*-nitro *p*-phenylenediamine, are diazotized with liquid nitrous anhydride, **diazoimines,** *e.g.*



are formed, and these yield stable acetyl derivatives (*Morgan* and others, J. C. S. 1917, **111**, 187; 1918, **113**, 588).

C. Azo-compounds, and Compounds intermediate between the Nitro- and Amino-compounds

While the reduction of nitro-compounds in acid solution leads to the aromatic amines, the use of alkaline reducing agents, such as sodium amalgam, zinc dust and caustic soda, and also potash and alcohol, gives rise for the most part to intermediate products, the azoxy-, azo-, and hydrazo-compounds:



Hydrazo-benzene, $C_6H_5NH \cdot NHC_6H_5$, and Aniline, $C_6H_5 \cdot NH_2$; and reduction in neutral solution yields phenyl-hydroxylamines, $C_6H_5 \cdot NH \cdot OH$.

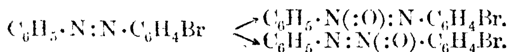
1. AZOXY-COMPOUNDS

The azoxy-compounds are mostly yellow or red crystalline substances which are obtained by the action of alcoholic

potash, and especially of potassium methoxide (B. **15**, 865), upon the nitro-compounds. Many of them may also be obtained by the oxidation of azo-compounds. They are neutral, and are very readily reduced to azo-compounds.

Azoxy-benzene, $(C_6H_5)_2N_2O$ (*Zinin*), forms pale-yellow needles melting at 36°, is insoluble in water, but dissolves readily in alcohol and ether. Concentrated sulphuric acid transforms it into the isomeric *p*-hydroxy-azo-benzene, $C_6H_5N:N\cdot C_6H_4\cdot OH$.

For a number of years the *sym.* structure $\begin{matrix} PhN \\ \vdots \\ PhN \end{matrix}\!\!>O$ was accepted. *Angeli's* demonstration of the formation of two isomeric azoxy-compounds from an *unsym.* azo-compound renders such a formula untenable.

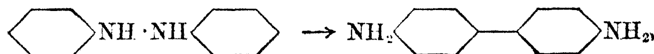


For confirmation cf. *Robinson* (J. C. S. 1917, **111**, **111**), who shows that one nitro group can be introduced quite readily into azoxy-veratrole, but that the introduction of a second can only be accomplished with difficulty.

2. HYDRAZO-COMPOUNDS

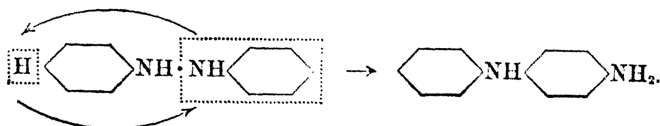
These are colourless crystalline neutral compounds, and, like the azo-compounds, cannot be volatilized without decomposition: *e.g.* hydrazo-benzene decomposes into azo-benzene and aniline when heated. They are obtained by the reduction of azo-compounds with ammonium sulphide or zinc dust and alkali, or by sodium hyposulphite. Oxidizing agents, such as ferric chloride, readily transform them into azo-compounds, a reaction which also occurs when the hydrazo-compounds are exposed to the air. Stronger reducing agents, *e.g.* sodium amalgam, convert them into amino-compounds.

Strong acids cause them to change into the isomeric derivatives of diphenyl (Chap. XXVII); thus from hydrazo-benzene and hydrochloric acid we obtain benzidine hydrochloride (the hydrocloride of *pp'*-diamino-diphenyl):

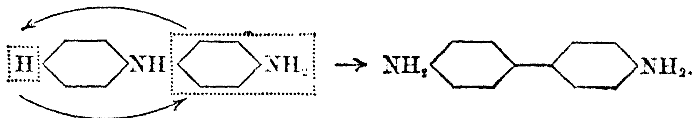


This rearrangement is typical, and is often observed in the case of aromatic compounds. It may be regarded as the

shifting or wandering of a radical—in this case the relatively complex $C_6H_5 \cdot NH$—from attachment to the side chain to direct attachment to the benzene nucleus, or, in other words, the $NH \cdot C_6H_5$ group exchanges place with the hydrogen atom in the *p*-position in the nucleus:

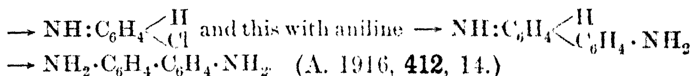


The operation is repeated,



and *pp'*-diamino-diphenyl, benzidine, is formed.

Another method of representing the change is by assuming the addition of HCl to the hydrazo-benzene and its resolution into $C_6H_5 \cdot NH_2$ and $C_6H_5 \cdot NHCl$. Then $C_6H_5 \cdot NHCl$



$\rightarrow NH:C_6H_4<^{H}_{Cl}$ and this with aniline $\rightarrow NH:C_6H_4<^{H}_{C_6H_4 \cdot NH_2}$
$\rightarrow NH_2 \cdot C_6H_4 \cdot C_6H_4 \cdot NH_2$. (A. 1916, **412**, 14.)

Other well-known examples of this are the transformation of methyl-aniline or dimethyl-aniline into *o*-toluidine and xylidene, and ultimately into mesidine (*Hofmann*, p. 396); the transformation of N-brominated amines or anilides, *e.g.* $C_6H_5 \cdot NBr \cdot COCH_3$ into $C_6H_4Br \cdot NH \cdot COCH_3$ (*Chattaway* and *Orton*, p. 395), of diacetylated amines, $C_6H_5 \cdot N(COCH_3)_2$, into ketonic substances, $CH_3 \cdot CO \cdot C_6H_4 \cdot NH \cdot CO \cdot CH_3$ (*Chattaway*, J.C.S. 1904, 386, 589, 1663), of phenyl-hydroxylamine into *p*-amino phenol (p. 426), and of diazo-amino-benzene into amino-azo-benzene (p. 421).

This molecular rearrangement does not take place if the hydrogen which occupies the para-position to the imino-group is replaced by other groups. In such cases a partial re-arrangement only occurs, and derivatives of diphenylamine are formed (B. **25**, 992, 1013, 1019); thus *p*-hydrazo-toluene, $CH_3 \cdot C_6H_4 \cdot NH \cdot NH \cdot C_6H_4 \cdot CH_3$, yields *o*-amino-di-*p*-tolylamine, $CH_3 \cdot C_6H_4 \cdot NH \cdot C_6H_3(CH_3) \cdot NH_2$. (Cf. *Jacobson*, B. 1893, **26**, 700; 1898, **31**, 890; A. 1895, **287**, 98.)

Hydrazo-benzene, *sym.-Diphenyl-hydrazine,* $C_6H_5\cdot NH\cdot NH\cdot C_6H_5$ (*Hofmann*), forms colourless plates of camphor-like odour, which are only slightly soluble in water, but dissolve readily in alcohol and ether; m.-pt. 131°. The imino-hydrogen atoms are replaceable by acetyl- or nitroso-groups.

When kept it undergoes spontaneous decomposition into a mixture of azo-benzene and aniline.

A group of compounds allied to the hydrazo-derivatives has been recently described by *Schlenk* (B. 1917, **50**, 276), *e.g.* **di-*p*-tolylammo-tetramethylammonium,** $NMe_4\cdot N(C_7H_7)_2$, which forms greenish-yellow crystals from pyridine. It is formed from NMe_4Cl and $(C_7H_7)_2NK$, is oxidized by the air, and is hydrolysed by water to ditolylamine and $NMe_4\cdot OH$. Its pyridine solution is an electrolyte.

3. AZO-COMPOUNDS

The azo-compounds are red or yellowish-red, crystalline, neutral substances, insoluble in water, but soluble in alcohol; some of them may be distilled without change. **Azo-benzene** itself (**benzene-azo-benzene,** $C_6H_5\cdot N:N\cdot C_6H_5$) crystallizes in large red plates, melts at 68°, and distils at 293°. Oxidizing agents convert them into azoxy-, and reducing agents, *e.g.* phenylhydrazine in the cold, into hydrazo- or amino-compounds. Chlorine and bromine act as substituents.

The so-called "mixed" azo-compounds, which contain both an alphyl and an aryl radical, are also known, *e.g.* **azo-phenyl-ethyl,** $C_6H_5\cdot N:N\cdot C_2H_5$, a bright-yellow oil (B. 1897, **30**, 793).

Modes of Formation.—1. By the cautious reduction of nitro- or azoxy-compounds, *e.g.* by means of sodium amalgam or of an alkaline solution of stannous oxide (B. **18**, 2912). 2. By distilling azoxy-benzene with iron filings. 3. By the oxidation of hydrazo-benzene. 4. By the oxidation of amino-compounds, *e.g.* together with azoxy-compounds by means of $KMnO_4$:



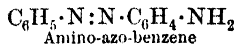
$$2C_6H_5\cdot NH_2 + 2O = C_6H_5\cdot N:N\cdot C_6H_5 + 2H_2O.$$

5. By the action of nitroso- upon amino-compounds in presence of acetic acid. In this way azo-benzene is obtained from nitroso-benzene and aniline acetate:

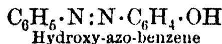


$$C_6H_5\cdot NO + NH_2\cdot C_6H_5 = C_6H_5\cdot N:N\cdot C_6H_5 + H_2O.$$

Amino- and hydroxy-derivatives of azo-benzenes are known, thus:—



$C_6H_5\cdot N:N\cdot C_6H_4\cdot NH_2$
Amino-azo-benzene



$C_6H_5\cdot N:N\cdot C_6H_4\cdot OH$
Hydroxy-azo-benzene

The former are at the same time bases and azo-compounds, and the latter azo-compounds and phenols (*i.e.* weak acids).

β-**Phenyl-hydroxylamine**, $C_6H_5 \cdot NH \cdot OH$, is formed when nitro-benzene is reduced with zinc dust and water in the presence of a mineral salt, *e.g.* $CaCl_2$, or in 80 per cent. yield by reducing the nitro compound in neutral media with hydrogen at room temperature in presence of palladised animal charcoal (B. 1922, 875). It is a colourless crystalline substance melting at 81°, and is relatively unstable. Aqueous solutions rapidly undergo oxidation on exposure to the air, yielding azoxy-benzene; oxidizing agents generally yield nitroso-benzene. Mineral acids immediately cause molecular rearrangement into *p*-amino-phenol, $NH_2 \cdot C_6H_4 \cdot OH$ (cf. p. 424). All the arylated *β*-hydroxylamines reduce *Fehling's* solution, and this affords a test for an aromatic nitro compound. If, after warming with water and zinc dust, a solution is obtained which reduces *Fehling's* solution, the presence of a nitro group in the original compound can be inferred.

D. Hydrazines

The aromatic hydrazines (*E. Fischer*) correspond with those of the fatty series (cf. p. 115). Phenyl-hydrazine, $C_6H_5 \cdot NH \cdot NH_2$, *s*-diphenyl-hydrazine or hydrazo benzene, $C_6H_5 \cdot NH \cdot NH \cdot C_6H_5$; unsym.-diphenyl-hydrazine, $(C_6H_5)_2N \cdot NH_2$, and phenylmethyl hydrazine, $(C_6H_5)(CH_3)N \cdot NH_2$, are all known.

Phenyl-hydrazine, $C_6H_5 \cdot NH \cdot NH_2$, forms a colourless crystalline mass, melting at 23° to a colourless oil, which quickly becomes brown from oxidation, and which is best distilled under reduced pressure. When kept or when heated it undergoes slow decomposition (*Chattaway*). It forms salts with mineral acids, *e.g.* the **hydrochloride**, $C_6H_5N_2H_3$, HCl (plates). Like all hydrazines, it has strong reducing power, reducing *Fehling's* solution even in the cold. It is readily destroyed by oxidation (*Chattaway*, C. N. 1911, **103**, 217), but is stable towards mild reducing agents. Energetic reducing agents convert it into aniline and ammonia. Gentle oxidation of the sulphate by means of HgO converts it into benzene-diazonium sulphate. It is *prepared*: (*a*) by reducing benzene-diazonium chloride with the calculated quantity of $SnCl_2$ and HCl:



$$C_6H_5N_2Cl + 4H = C_6H_5 \cdot NH \cdot NH_2, HCl;$$

(*b*) by reducing potassium diazo-benzene-sulphonate, $C_6H_5 \cdot N:N \cdot SO_3K$ (from $C_6H_5N_2Cl$ and K_2SO_3), with zinc dust and

acetic acid to potassium phenyl-hydrazine-sulphonate, $C_6H_5 \cdot NH \cdot NH \cdot SO_3K$, which is then hydrolysed to phenyl-hydrazine and sulphuric acid:



$$C_6H_5 \cdot NH \cdot NH \cdot SO_3K + HCl + H_2O = C_6H_5 \cdot NH \cdot NH_2, HCl + KHSO_4.$$

Alkyl and acyl derivatives of phenyl-hydrazine are known; the former (mono-alkylated derivatives only) are obtained by the action of alkyl iodides on the base or its metallic derivatives. **Phenyl-methyl-hydrazine**, which can be obtained in this way, is largely used for differentiating ketoses and aldoses (p. 312); its constitution follows from its formation by the reduction of nitroso-methyl-aniline, $\frac{C_6H_5}{CH_3} > N \cdot NO$. Both mono- and diacyl derivatives are known. The mono-acyl derivatives or **hydrazides** (cf. Amides, Anilides) are obtained by the action of the acid or acid anhydrides on the base; they give a violet-red coloration with sulphuric acid and dichromate of potash, and can be used for isolating acids which are readily soluble (B. **22**, 2728), *e.g.* **acetylphenyl-hydrazide**, $C_6H_5 \cdot NH \cdot NH \cdot CO \cdot CH_3$; m.-pt. 128°.

The base is an important and often an exceedingly delicate reagent for aldehydes and ketones, combining with them to hydrazones, with elimination of water (cf. pp. 134 and 142). Most of these compounds are solid and crystalline, and are therefore eminently suited for the recognition of aldehydes and ketones. With certain sugars it yields phenyl-hydrazones, but with an excess of the base, osazones (p. 311) are formed. Diketones, keto-aldehydes, &c., also yield osazones.

With ethyl aceto-acetate, phenyl-hydrazine forms pyrazole derivatives, *e.g.* phenyl-methyl-pyrazolone, the methyl derivative of which is antipyrine (see p. 238).

Diphenyl-hydrazine, $(C_6H_5)_2N \cdot NH_2$, is an oily base which boils without decomposition, and, like phenyl-hydrazine, is easily oxidized; it only reduces *Fehling's* solution, however, when warmed. It is obtained by reducing diphenyl-nitrosamine, $(C_6H_5)_2N \cdot NO$, with zinc dust and acetic acid. M.-pt. 34°. Like phenyl-hydrazine, it yields characteristic hydrazones and osazones with the sugars.

p-**Bromo-phenyl-hydrazine**, $C_6H_4Br \cdot NH \cdot NH_2$, and *p*-**nitro-phenyl-hydrazine** are often used in isolating carbonyl compounds, as the hydrazones crystallize well (B. 1899, **32**, 1806).

Bis (methyl-hydrazine-phenyl) methane, $CH_2(C_6H_4 \cdot NMe \cdot NH_2)_2$, is recommended as a reagent for characterizing alde-

hydes, as it reacts only slowly with ketones, with the exception of α-ketonic acids. (*Braun*, B. 1908, **41**, 2169; *Harries*, Abs. 1917, **i**, 210.)

For relative rates of reduction of methylated phenylhydrazines, cf. J. pr., 1918, **97**, 61, 336.

Ditertiary-hydrazines, $R_2N \cdot NR_2$, are formed by the oxidation of secondary amines with lead dioxide. Many of them dissolve in benzene, giving coloured solutions, which it is presumed contain free radicals, $:NR_2$, together with tertiary amines, NR_3. The existence of the free radical is supported by the fact that when kept for some time the chief products are tertiary amines and azo-derivatives, RN:NR. Tri-phenylhydrazine in boiling xylene gives diphenylamine and NPh, which polymerizes to azo-benzene (*Wieland*). The spontaneous decomposition of hydrazo-benzene (p. 425) into aniline and azo-benzene is a unimolecular reaction, and probably consists in the dissociation into aniline and :NPh and the polymerization of the latter to azo-benzene (*Stieglitz* and *Curme*, B. 1913, **46**, 911; cf. *Wieland*, *ibid.* 1915, **48**, 1094).

E. Azo-dyes

A number of compounds derived from azo-benzene and its homologues are largely used as dyes, under the name of azo-dyes. These compounds are either basic and contain NH_2 or $N(CH_3)_2$ groups, or are acidic and then contain either phenolic, OH, or sulphonic, $SO_2 \cdot OH$, and phenolic groups. Azo benzene itself is a highly-coloured substance, but is not a dye. In order that a coloured substance shall be a dye, it is essential that the colour it imparts to a fabric shall not be removed by washing or treatment with soap. According to *O. Witt*, when certain characteristic groups known as **chromophores**, among which are ·N:N and NO_2, are present, the compound is coloured or is a **chromogene**; and when, in addition to the chromophore, a strongly basic (*e.g.* NH_2) or acidic group (*e.g.* ·OH or $\cdot SO_2 \cdot OH$) is also present, we obtain a **dye**, *e.g.*:

Chromogenes.	Dyes
Nitro-benzene	Nitraniline, $NO_2 \cdot C_6H_4 \cdot NH_2$;
Nitro-benzene	Picric acid. $(NO_2)_3 \cdot C_6H_2 \cdot OH$:
Azo-benzene	*p*-Hydroxy-azo-benzene, $C_6H_5 \cdot N:N \cdot C_6H_4 \cdot OH$.

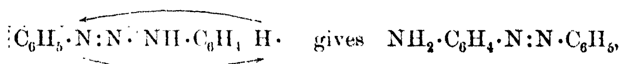
The majority of dyes, when reduced, yield colourless compounds—**leuco-compounds**—which on oxidation are converted into the original dyes.

With regard to the theory of the process of dyeing fabrics,

there are still two distinct schools. According to one, the process consists in the formation of definite compounds of the basic or acidic dye with acidic or basic constituents of the fabric dyed. According to the other, the operation is largely a physical one, and the dyed fabric may be regarded as a solid solution.

In most cases, silk and woollen—and in a few cases cotton—fabrics can be dyed by direct immersion in a solution of the dye; but, as a rule, cotton will not dye directly, but requires previous treatment with a **mordant**. The object of the mordant is to deposit some substance on the fabric which will afterwards combine with or fix the dye. The chief mordants employed for acid dyes are the feeble bases aluminic, chromic, or ferric hydroxides, obtained by immersing the fabric in a solution of the metallic acetate, and then subjecting to the action of steam. The product formed by the action of the dye on the mordant is known as a **lake**, and the same dye can give rise to different-coloured lakes, according to the mordant used. When basic dyes are employed for cotton goods, the fabric is usually mordanted with tannic acid. Stannic hydroxide obtained from such a salt as $SnCl_4, 2NH_4Cl$ is also used as a mordant.

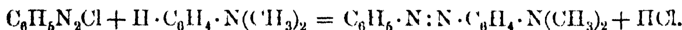
p-**Amino-azo-benzene** is the parent substance of the dyes known as **chrysoidines**. It may be obtained (1) by nitrating azo-benzene and then reducing (this indicates its constitution as an amino-derivative of azo-benzene); (2) by molecular rearrangement of diazo-amino-benzene (p. 421):



$$C_6H_5 \cdot N:N \cdot NH \cdot C_6H_4 H \quad \text{gives} \quad NH_2 \cdot C_6H_4 \cdot N:N \cdot C_6H_5,$$

another example of the wandering of a radical from a side chain into the benzene nucleus. The amino-group occupies the *p*-position with respect to the azo-group.

Substituted amino-azo-benzenes, *e.g.* dimethyl-amino-azo-benzene, are obtained directly by the action of a diazonium salt on a tertiary amine:



$$C_6H_5N_2Cl + H \cdot C_6H_4 \cdot N(CH_3)_2 = C_6H_5 \cdot N:N \cdot C_6H_4 \cdot N(CH_3)_2 + HCl.$$

Assuming the *Blomstrand* formula for the diazonium salt, the reaction is probably first additive, and then HCl is eliminated:



$$\begin{matrix} C_6H_5 \\ Cl \end{matrix} \!\!>\! N:N \rightarrow \begin{matrix} C_6H_5 \cdot N:N \cdot C_6H_4 \cdot N(CH_3)_2 \\ \wedge \\ ClH. \end{matrix}$$

The azo-group always takes up the *p*-position with respect to the substituted amino-group if this position is free. If, however, the *p*-position is already substituted, a dye is not formed, or is formed very incompletely, and the *o*-position is taken up.

The chrysoidines are coloured yellow to brown, and, as they contain amino- or substituted amino-groups in the molecule, are basic, and form well-defined salts with mineral acids.

Among the simplest chrysoidines we have:—

Aniline yellow, the hydrochloride of *p*-amino-azo-benzene. It is now very little used.

Chrysoidine, or 2:4-*diamino-azobenzene hydrochloride*, $C_6H_5 \cdot N:N \cdot C_6H_3(NH_2)_2$, HCl [$N_2:(NH_2)_2$ = 1:2:4]. It dyes silk and wool directly an orange-red colour.

Bismarck brown, or 3′:2:4-*triamino-azo-benzene hydrochloride*, $NH_2 \cdot C_6H_4 \cdot N:N \cdot C_6H_3(NH_2)_2$, HCl, is obtained by diazotizing *m*-phenylenediamine and coupling the tetrazonium salt with two more molecules of the base.

The brown coloration obtained by the addition of a few drops of dilute nitrous acid solution to *m*-phenylenediamine is due to the formation of Bismarck brown or a related substance. The hydrochloride crystallizes in reddish-brown plates.

Many of the chrysoidine dyes are sulphonated derivatives of amino-azo-benzene. As an example, we have **methyl orange**, which is the sodium salt of **helianthine** or *p*-dimethamino-azo-benzene-*p*-sulphonic acid, $(CH_3)_2N \cdot C_6H_4 \cdot N:N \cdot C_6H_4 \cdot SO_2 \cdot OH$. It is largely made use of as an indicator in volumetric analysis, as it is not affected by weak acids, *e.g.* carbonic, but is an extremely delicate reagent for the feeblest alkalis.

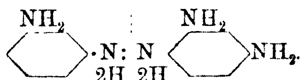
The dyes known as **tropæolines** are derivatives of *p*-hydroxy-azo-benzene. Such compounds are obtained by adding the cold diazotized solution to an *alkaline* solution of a phenol. The dye is then salted out by the addition of sodium chloride and collected. The reaction is often made use of in testing for a primary aromatic amine (p. 417), as the precipitates produced are usually coloured bright red. The azo-group invariably occupies the *p*-position with respect to the OH group, unless this is already substituted.

p-**Hydroxy-azo-benzene** crystallizes in brick-red prisms, and is a yellowish-red dye.

Resorcin yellow, $OH \cdot SO_2 \cdot C_6H_4 \cdot N:N \cdot C_6H_3(OH)_2$, 2:4-*dihydroxy-azo-benzene-4′-sulphonic acid*, obtained by coupling a

diazotized solution of sulphanilic acid with an alkaline solution of resorcinol, is known as Tropæolin O.

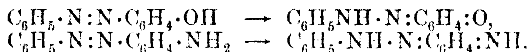
The *constitution* of an azo-dye can usually be determined by an examination of its decomposition products, especially the products formed by energetic reduction; *e.g.* Bismarck brown, on reduction with tin and hydrochloric acid, yields a mixture of 1:3-diamino- and 1:2:4-triamino-benzene:



Bis-azo-dyes.—Certain well-known dyes, *e.g.* **Biebrich scarlet,** contain two azo-groups. Such can be obtained by diazotizing an amino-derivative of azo-benzene, and then coupling it with a tertiary amine or with a phenol, and we thus obtain compounds of the type $C_6H_5·N:N·C_6H_4·N:N·C_6H_4·OH$.

Another type of bis-azo-compound is formed by coupling a diamine or dihydric phenol with 2 mols. of a diazonium salt.

Many amino- and hydroxy-azo-derivatives react as tautomeric substances, especially those which contain an NH_2 or OH group in the ortho-position with respect to the N_2 radical. These react as though they were quinone hydrazones or quinone-imide derivatives, *e.g.*:



$$C_6H_5·N:N·C_6H_4·OH \rightarrow C_6H_5NH·N:C_6H_4:O,$$
$$C_6H_5·N:N·C_6H_4·NH_2 \rightarrow C_6H_5·NH·N:C_6H_4:NH.$$

For a general summary compare *Auwers* (A. 1908, **360,** 11), and *Smith* and *Mitchell* (J. C. S. 1908, **93**, 842; 1909, **95,** 1430). The general conclusion drawn is that all the compounds, both para and ortho, are true hydroxy-azo-compounds.

According to *Hantzsch*, many of the hydroxy-azo-compounds are pseudo-acids (p. 391), *i.e.* the hydrogen compound is the quinone hydrazone; but in the formation of a salt, intramolecular rearrangement occurs, *e.g.*:



$$C_6H_5·NH·N:C_6H_4:O \longrightarrow C_6H_5·N:N·C_6H_4·ONa.$$

For further types of azo-dyes cf. Chap. LV.

F. Phosphorus Compounds, &c.; Organo-Metallic Derivatives

The phosphorus, &c., compounds of the fatty series have their analogues in corresponding compounds of the aromatic; these latter have been investigated by *Michaelis* and his

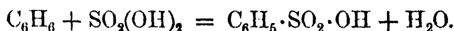
pupils (A. **181**, **188**, **201**, **212**, and **229**; B. **28**, 2205): for instance, **phenyl phosphine**, $C_6H_5 \cdot PH_2$; **phenyl phosphinic acid**, $C_6H_5PO(OH)_2$; **phosphenyl chloride**, $C_6H_5 \cdot PCl_2$; **phosphino-benzene**, $C_6H_5PO_2$; and **phospho-benzene**, $C_6H_5P:P \cdot C_6H_5$ (these two last being analogous to nitro- and to azo-benzene). Some of those compounds are solid, and they are less volatile and more stable than the corresponding aliphatic compounds. For important arsenic compounds see Chap. LV.

Aromatic Organo-Metallic Compounds. — Mercury, tin, lead, tellurium, and magnesium yield phenyl derivatives. **Mercury phenyl**, $Hg(C_6H_5)_2$, is obtained by the action of sodium amalgam of bromobenzene. It is relatively stable. Numerous compounds of the type of **phenyl magnesium bromide**, $C_6H_5 \cdot Mg \cdot Br$, have been prepared, and are used as synthetical reagents (cf. p. 384). For general discussion on organo-metallic compounds, cf. *Zeltner*, J. pr., 1908, **77**, 393.

XXIII. AROMATIC SULPHONIC ACIDS

The aromatic sulphonic acids are very similar in properties to the sulphonic acids of the fatty series, but can be obtained much more readily. One of the characteristic properties of benzene and its derivatives is the readiness with which they react with concentrated sulphuric acid, yielding sulphonic acids. In some cases fuming sulphuric acid is used; in others sulphuryl chloride, $OH \cdot SO_2 \cdot Cl$.

Benzene-sulphonic acid, $C_6H_5 \cdot SO_2 \cdot OH$ (*Mitscherlich*, 1834), is formed when benzene is heated with concentrated sulphuric acid for some hours:

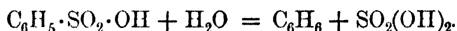


$$C_6H_6 + SO_2(OH)_2 = C_6H_5 \cdot SO_2 \cdot OH + H_2O.$$

As in the case of ethyl hydrogen sulphate, advantage is taken of the solubility of its barium, calcium, or lead salt to separate it from the excess of sulphuric acid; or its sodium salt is separated by the addition of sodium chloride.

It crystallizes in small plates containing $1\frac{1}{2}\,H_2O$, deliquesces in the air, and is readily soluble in alcohol. The **barium salt** crystallizes in glistening mother-of-pearl plates containing $1H_2O$. It is very stable, and is not hydrolysed when boiled with alkalis or acids (cf. Ethyl hydrogen sulphate). It is, however,

decomposed into benzene and sulphuric acid when heated with hydrochloric acid at 150°, or with water vapour at a high temperature (cf. p. 375):



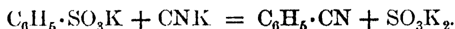
$$C_6H_5 \cdot SO_2 \cdot OH + H_2O = C_6H_6 + SO_2(OH)_2.$$

When fused with alkali, it yields phenol in the form of its potassium salt:



$$C_6H_5 \cdot SO_3K + 2KOH = C_6H_5 \cdot OK + SO_3K_2 + H_2O,$$

and when distilled with potassium cyanide, it yields benzonitrile:



$$C_6H_5 \cdot SO_3K + CNK = C_6H_5 \cdot CN + SO_3K_2.$$

With PCl_5 the OH group present in the sulphonic acid radical is replaced by chlorine, and **benzene-sulphonic chloride** is formed:



$$C_6H_5 \cdot SO_2OH + PCl_5 = C_6H_5 \cdot SO_2Cl + POCl_3 + HCl.$$

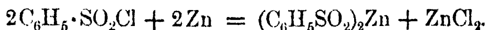
This is an oil, insoluble in water; it melts at 14·5°, and boils at 120° (under 10 mm. pressure); as an acid chloride it is reconverted into sulphonic acid by hot water, into the corresponding esters by alcohols, and into **benzene-sulphonamide**, $C_6H_5 \cdot SO_2 \cdot NH_2$ (lustrous mother-of-pearl plates melting at 150°), by ammonia. This compound can be sublimed, and corresponds with other amides in its properties. The amido-group, however, is so affected by the strongly acidifying action of the SO_2 group that its hydrogen is replaceable by metals, and the sulphonamides consequently *dissolve in aqueous solutions of alkali hydroxides.*

The sulphonamides are largely made use of in distinguishing the various sulphonic acids. These acids themselves are difficult to purify, as a rule do not crystallize well, and have no definite melting-point. The sulphonamides, on the other hand, crystallize readily, and have sharp melting points. The sodium salt of the acid is treated with PCl_5, and the chloride thus obtained is warmed with ammonium carbonate.

Benzene-sulphonic chloride likewise yields sulphonamides with primary and secondary amines, $C_6H_5 \cdot SO_2 \cdot NHR$ and $C_6H_5 \cdot SO_2 \cdot NRR'$, the former of these being soluble in alkali, but the latter insoluble. Tertiary amines do not, of course, give sulphonamides. This serves as the basis of a method for separating primary, secondary, and tertiary bases, especially

when β-anthraquinone **sulphonic chloride** is used (*Hinsberg*, B. **23**, 2962; 1900, **33**, 477, 557, 3526; **38**, 906).

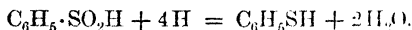
When benzene-sulphonic chloride is treated with zinc dust, zinc benzenesulphinate is formed:



$$2C_6H_5 \cdot SO_2Cl + 2Zn = (C_6H_5SO_2)_2Zn + ZnCl_2.$$

An alkaline sulphinate is also produced (along with phenyl disulphide as by-product) when benzene-sulphonic chloride is treated with thio-phenol in presence of alkali.

Benzene-sulphinic acid crystallizes in large glistening prisms, readily soluble in hot water, alcohol, and ether. It possesses reducing properties, and is itself converted into thio-phenol by nascent hydrogen:



$$C_6H_5 \cdot SO_2H + 4H = C_6H_5SH + 2H_2O.$$

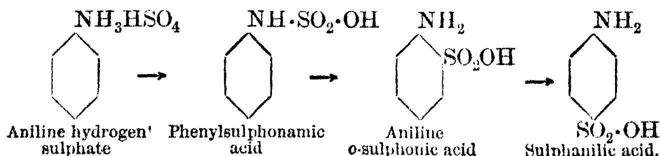
Thio-phenols can also be obtained by reducing the sulphonamides derived from primary arylamines or the arylsulphonic chlorides with HI and PH_4I. The sulphonic acids and their esters cannot be reduced by this method (*Fischer*, B. 1915, **48**, 93).

Sulphinic acids can be synthesized from *Grignard* reagents and SO_2.

Substitution may be effected in benzene-sulphonic acid by chlorine, bromine, and the groups NO_2 and NH_2.

The **nitro-benzene-sulphonic acids**, $NO_2 \cdot C_6H_4 \cdot SO_3H$, are obtained by nitrating benzene-sulphonic acid or by sulphonating nitro-benzene, the *m*-compound preponderating. Reducing agents convert them into the—

Amino-benzene-sulphonic acids, $NH_2 \cdot C_6H_4 \cdot SO_3H$. The *p*-compound, which is termed **sulphanilic acid**, is obtained by heating aniline sulphate at 180°–200° (*Gerhardt*, 1845); also by reducing *p*-nitro-benzene-sulphonic acid. The conversion of aniline sulphate into sulphanilic acid proceeds as follows:—



Aniline hydrogen sulphate — Phenylsulphonamic acid — Aniline o-sulphonic acid — Sulphanilic acid.

(Cf. *Bamberger*, B. 1897, **30**, 2274.) It crystallizes in rhombic plates ($+H_2O$), sparingly soluble in water, forms metallic salts,

e.g. sodium sulphanilate, $NH_2 \cdot C_6H_4 \cdot SO_3Na + 2H_2O$ (large plates), but does not combine with acids. The formula $C_6H_4 <^{NH_3}_{SO_3}>$ possibly expresses the constitution of sulphanilic acid. The *m*-acid, also termed **metanilic acid**, is employed in the preparation of azo-dyes, *e.g.* metaniline yellow; it crystallizes in fine needles or prisms.

Diazo-benzene-sulphonic acid, $C_6H_4 <^{N:N}_{SO_3}>$ (the anhydride of $C_6H_4 <^{N:N \cdot OH}_{SO_3H}$), is obtained by adding a mixture of sulphanilate and nitrite of sodium to dilute sulphuric acid. It forms colourless needles, sparingly soluble in water, shows all the reactions of the diazo-compounds, and is of great importance for the preparation of azo-dyes.

Benzene-disulphonic acids, $C_6H_4(SO_3H)_2$ (principally meta-), and **benzene-trisulphonic acids,** $C_6H_3(SO_3H)_3$, result from the energetic sulphonation of benzene with fuming sulphuric acid. The former exist, of course, in three isomeric modifications. When they are distilled with KCN, they yield the compounds $C_6H_4(CN)_2$, the nitriles of the phthalic acids; when fused with KOH, the *m*-disulphonic acid changes into resorcinol (*m*-dihydroxy-benzene), $C_6H_4(OH)_2$.

Almost all the homologues of benzene, with the exception of hexamethyl-benzene, yield sulphonic acids. From toluene are obtained the *o*-, *m*-, and *p*-toluene sulphonic acids, $CH_3 \cdot C_6H_4 \cdot SO_3H$ (*Hollemann* and *Caland*, B. 1911, **44**, 2504). Of these it is the *p*-acid which is formed in largest quantity directly; its potassium salt crystallizes beautifully.

The sulphonic acids of the three xylenes, the **xylene-sulphonic acids,** $C_6H_3(CH_3)_2SO_3H$, serve for the separation of these isomers from each other; and the power of crystallization of the salts or amides of the sulphonic acids of the higher benzene homologues is frequently made use of for the recognition and separation of these hydrocarbons.

The N-halogenated sulphonamides have received much attention within recent years. The compounds $C_6H_5 \cdot SO_2 \cdot NCl \cdot CH_3$ and $C_6H_5 \cdot SO <^{OK}_{NCl}$ were prepared by *Chattaway* (J. C. S. 1905, 145), the former by the action of hypochlorous acid on the corresponding amide and the latter by the action of warm potassium hydroxide on the dichloride, $C_6H_5 \cdot SO_2 \cdot NCl_2$, obtained from the amide and hypochlorous acid. Cf. Chap. LIV, Antiseptics.

XXIV. PHENOLS

The hydroxylic derivatives of benzene and its homologues are usually divided into (*a*) phenols and (*b*) aromatic alcohols. The phenols all contain the hydroxyl group or groups directly attached to the benzene nucleus, *e.g.* $C_6H_5(OH)$, $C_6H_4(OH)_2$, whereas in the alcohols the hydroxyl group is present in a side chain, *e.g.* $C_6H_5 \cdot CH_2 \cdot OH$.

One important point of difference between the phenols and alcohols is the more pronouncedly acidic nature of the phenol. The aromatic alcohols closely resemble those of the aliphatic series, but the phenols react as feeble acids, the hydroxylic hydrogen being displaced by the action of sodium or potassium hydroxide.

The phenols are either liquid or solid compounds, and are often characterized by a peculiar odour, *e.g.* carbolic acid and thymol. Most of them can be distilled without decomposition, and all are readily soluble in alcohol or ether; some dissolve easily in water, others less readily, the solubility tending to increase with the number of hydroxyl groups present in the molecule. Many of them are antiseptics, *e.g.* phenol, creosol, thymol, and resorcinol.

The phenols are usually divided into mono-, di-, tri- or tetrahydric, according to the number of OH groups present in the molecule.

Behaviour.—1. Like the alcohols, the phenols are capable of forming ethers such as anisole, $C_6H_5 \cdot O \cdot CH_3$, esters, *e.g.* phenyl acetate, $C_6H_5 \cdot O \cdot CO \cdot CH_3$, and phenyl hydrogen sulphate, $C_6H_5O \cdot SO_2 \cdot OH$, thio-compounds, *e.g.* thiophenol, $C_6H_5 \cdot SH$, &c.

They can only be compared with the tertiary alcohols, since they cannot, like the primary or secondary alcohols, yield acids or ketones containing an equal number of carbon atoms in the molecule upon oxidation.

2. The phenols are weak acids, and form salts known as **phenates** or **phenoxides**, *e.g.* $C_6H_5 \cdot OK$, potassium phenate or potassium phenoxide; most of the salts are readily soluble in water, and far more stable than the alcoholates, with which they correspond.

In aqueous solutions the salts are largely hydrolysed, and are decomposed by carbon dioxide, as the phenols are extremely feeble acids comparable with hydrocyanic acid (cf. *Walker*, Phys. Chem., chapter xxiv). The acid character of the

Monohydric Phenols

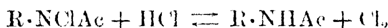
Formula	Name.	Positions of Substituents OH in 1.	Melting-point.	Boiling-point.	Specific Gravity.
$C_6H_5 \cdot OH$	Phenol	...	42·5°	183°	1·039
$CH_3 \cdot C_6H_4 \cdot OH$	*o*-Cresol	1:2	30°	191°	1·043
	m-Cresol	1:3	4°	203°	1·035
	p-Cresol	1:4	36°	202°	1·034
$(CH_3)_2C_6H_3 \cdot OH$	adj.-*o*-Xylenol	1:2:3	73°	213°	...
	asym.-*o*-Xylenol	1:3:4	65°	222°	...
	p-Xylenol	1:2:5	75°	209°	...
$(CH_3)_3C_6H_2 \cdot OH$	Pseudo-cumenol	1:2:4:5	73°	234°	...
$(CH_3)_2CH \cdot C_6H_3(CH_3)(OH)$	Carvacrol	1:2:4	0·5°	237°	0·979
	Thymol	1:3:6	51°	232°	0·982
$C_6H_3(OH)(OMe)(CH_2 \cdot CH{:}CH_2)$	Eugenol	1:2:4	—	252°	1·070
$C_6H_4(OH)_2$	Catechol	1:2	104°	240°	...
	Resorcinol	1:3	119°	276°	...
	Quinol	1:4	169°	...	..
$CH_3 \cdot C_6H_3 \cdot (OH)_2$	Orcinol	1:3:5	107°	288°	...

Trihydric Phenols

Formula	Name.	Positions of Substituents OH in 1.	Melting-point.	Boiling-point.	Specific Gravity.
$C_6H_3(OH)_3$	Pyrogallol	1:2:3	132°	...	...
	Hydroxyquinol	1:2:4	140°	...	...
	Phloroglucinol	1:3:5	217–219°	...	...

phenols is considerably increased by the entrance of negative groups, especially NO_2, into the molecule. (See Picric acid; also Abst. 1903, 1, 754.)

3. The presence of NH_2, or OH groups in the benzene nucleus renders compounds much more reactive towards halogens, nitric acid, sulphuric acid, oxidizing agents, &c. With polyamines and aminophenols the reactivity is such that the compounds undergo spontaneous oxidation on exposure to the air. The reactivity with chlorine is so great that frequently compounds of this type cannot be chlorinated by the usual methods. *Orton* and *King* (J. C. S. 1911, 1185; 1927, 986; 1928, 998; 1930, 37) have introduced a method based upon the fact that the reversible reaction:



$$R{\cdot}NClAc + HCl \rightleftharpoons R{\cdot}NHAc + Cl_2$$

proceeds from left to right in the presence of glacial acetic acid, and thus by taking very dilute solutions of hydrochloric acid, *e.g.* 0·021 *N*, the concentration of the chlorine is kept so low that chloro-derivatives are obtained free from products of oxidation. Cresols can be chlorinated in the same manner. The acetyl derivative generally used is 2:4-dichloro-acetylchloranilide, and if the theoretical amount of this compound is used the reaction proceeds to completion, as hydrogen chloride is formed by the action of the chlorine on the amine or phenol.

The method has been used for determining the velocities of many chlorinations (J. C. S. 1928, 782, 1006, 3073).

4. Many phenols give characteristic colorations with ferric chloride in neutral solution, *e.g.* phenol and resorcinol violet, catechol green, and orcinol blue-violet; while pyrogallol yields a blue colour with ferrous sulphate containing a ferric salt, and a red one with ferric chloride. Bleaching-powder and iodine solution, in certain cases, also give particular coloration.

5. *Liebermann's Reaction.*—When the phenols are mixed with concentrated H_2SO_4 and a drop of nitrite solution or of a nitrosamine, they yield intensely coloured solutions which turn to a deep-blue or green when diluted and rendered alkaline with potash.

6. The sodium and potassium salts of the phenols react with CO_2 (*Kolbe*) or with $COCl_2$, with formation of aromatic hydroxy-acids, *e.g.* salicylic acid (see this). Cf. also Chap. XXV, D.

7. The phenols couple with diazonium salts to form azo-dyes (Chap. XXII, E); heated with benzo-trichloride, $C_6H_5{\cdot}CCl_3$, they yield the aurin dyes, and with phthalic acid, phthaleins.

8. When heated with zinc dust, the phenols are converted into the corresponding hydrocarbons (*Baeyer*).

9. When heated with the additive compounds of zinc chloride and ammonia or calcium chloride and ammonia, the OH is replaced by NH_2 (cf. p. 396; also B. **19**, 2901).

10. Heating with phosphorus pentachloride partially converts the phenols into chlorinated hydrocarbons, and heating with P_2S_5 into thio-phenols.

Occurrence.—Many individual phenols are found in the vegetable and animal kingdoms, and also in coal-tar.

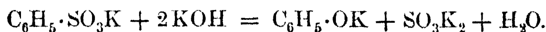
Constitution.—The hydroxyl-groups in phenol, $C_6H_5 \cdot OH$, and in the di- and polyhydroxy-benzenes, containing six carbon atoms, are linked to the benzene nucleus. That this is also the case in the homologues of these compounds follows: (*a*) from their completely analogous reactions; (*b*) from their behaviour upon oxidation. Thus, when oxidized, *m*-cresol yields *m*-hydroxy-benzoic acid, and hence the OH is present in the benzene nucleus and not in the side chain, and must be in the *m*-position with respect to the methyl group.

A. Monohydric Phenols

Modes of Formation.—1. Many phenols are formed during the destructive distillation of the more complex carbon compounds, especially of wood and coal; they are therefore present in wood- and coal-tars. The latter contains more especially phenol and its homologues, cresol, &c.; the former, among other products, the methyl ethers of polyhydric phenols, *e.g.* guaiacol, $C_6H_4 \cdot (OH)(O \cdot CH_3)$, and its homologue creosol, $C_6H_3(CH_3)(OH)(O \cdot CH_3)$.

The phenols are isolated from coal-tar, &c., by shaking with sodium hydroxide solution, in which they dissolve, saturating the alkaline solution with hydrochloric acid, and purifying the precipitated phenols by fractional distillation.

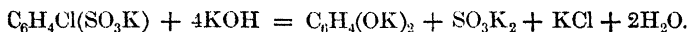
2. Phenols are formed together with an alkali sulphite when salts of sulphonic acids are fused with potassium or sodium hydroxides (*Kekulé*, *Wurtz*, *Dusart*, 1867):



$$C_6H_5 \cdot SO_3K + 2KOH = C_6H_5 \cdot OK + SO_3K_2 + H_2O.$$

In the laboratory nickel or silver basins are used for this fusion, and on the large scale iron boilers, &c. The alkali salts of the phenols are formed, and the free phenols may be liberated, by the addition of mineral acid. The chlorinated

sulphonic acids and the chlorinated phenols also exchange the halogen for hydroxyl when fused with potash:

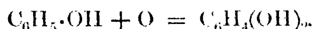


$$C_6H_4Cl(SO_3K) + 4KOH = C_6H_4(OK)_2 + SO_3K_2 + KCl + 2H_2O.$$

In certain cases intramolecular rearrangement occurs during this fusion, *e.g.* all three bromo-benzene-sulphonic acids yield *m*-dihydroxy-benzene (resorcinol) when fused with potash.

3. They are formed when aqueous solutions of diazonium salts are heated (*Griess*; cf. p. 415). As a rule, a very dilute sulphuric acid solution is employed.

4. Phenol is produced from benzene by the action of ozone or hydrogen peroxide, and also by that of the oxygen of the air in presence of caustic soda solution or of aluminium chloride. In an analogous manner di- and even trihydroxy-benzene may be obtained by fusing phenol with potash:



$$C_6H_5 \cdot OH + O = C_6H_4(OH)_2.$$

5. The phenols cannot be prepared from chloro-, bromo-, or iodo-benzene in the same way as the alcohols from alkyl chlorides, bromides, or iodides, the halogen being bound too firmly to the benzene nucleus. The bromo-compounds when heated with alkalis under a pressure of 20 atmospheres yield metallic phenoxides. If nitro-groups are present in *o*- or *p*-positions, an exchange of this kind can be effected by heating with aqueous sodium or potassium hydroxides; *s*-trinitro-chloro-benzene reacts with water alone:



$$C_6H_2Cl(NO_2)_3 + HOH = C_6H_2(OH)(NO_2)_3 + HCl.$$

Similarly, the amino-group in amino-compounds may be replaced by hydroxyl by means of boiling alkalis, provided nitro-groups are also present in certain position; thus *o*- and *p*- (not *m*-) dinitro-aniline yield dinitro-phenols, a reaction which corresponds with the saponification of acid amides.

6. Phenols are also formed when salts of the aromatic hydroxy-acids are distilled with lime, or when their silver salts are carefully heated:



Gallic acid, $C_6H_2(OH)_3 \cdot CO_2H = CO_2 + C_6H_3(OH)_3$, Pyrogallol.

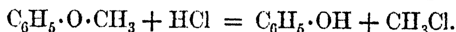
7. Homologues of phenol are readily prepared by reducing certain aromatic hydroxy-ketones or aldehydes with zinc amalgam and HCl. Thus p-$OH \cdot C_6H_4 \cdot CHO$ gives p-$OH \cdot C_6H_4 \cdot CH_3$ and $OH \cdot C_6H_4 \cdot CO \cdot CH_3$ gives $OH \cdot C_6H_4 \cdot CH_2 \cdot CH_3$.

Phenol, *Carbolic acid, hydroxy-benzene,* C_6H_5OH, was dis-

covered in 1834 by *Runge* in coal-tar. It occurs in the urine of the herbivora and in human urine as phenyl hydrogen sulphate, also in cocoanut-shell tar, and in bone-oil. It forms long, colourless needles, melts at 42°, boils at 181°, is soluble in fifteen parts of water at 16°, and itself dissolves some water, a small percentage of the latter sufficing to liquefy the crystalline phenol. Alcohol and ether dissolve it readily. It is hygroscopic, and acquires a reddish colour in the air owing to the presence of impurities, possesses a characteristic odour and burning taste, is poisonous, acts as a splendid antiseptic, and exerts a strongly corrosive action upon the skin. As a very feeble acid it dissolves readily in caustic potash solution, but not in the carbonate. Ferric chloride colours the aqueous solution violet, while a pine shaving moistened with hydrochloric acid is turned greenish-blue by phenol.

Hexahydro-phenol, Cyclohexanol, $C_6H_{11}\cdot OH$, made by the catalytic reduction of phenol has b.p. 160° and is a commercial solvent.

Anisole, or *Phenyl methyl ether*, $C_6H_5\cdot O\cdot CH_3$, and **phenetole,** or *phenyl ethyl ether*, $C_6H_5\cdot O\cdot C_2H_5$, are best obtained by heating phenol and caustic soda with methyl or ethyl sulphates or halides; the former is also obtained by distilling anisic acid with lime. They are liquids of ethereal odour which boil at a lower temperature than phenol, just as ether has a lower boiling-point than alcohol. They are very stable neutral compounds, which are not readily hydrolysed by acids or alkalis; when heated with HI to 140°, or with HCl to a higher temperature, or with aluminium chloride, they yield phenol:



$$C_6H_5\cdot O\cdot CH_3 + HCl = C_6H_5\cdot OH + CH_3Cl.$$

When methylating phenols with methyl sulphate better yields are given by using NaOH than by KOH, but for esters potash is preferable (*Klemens*, Mon., 1918, **38**, 553).

Phenyl ether, *Diphenyl oxide*, $(C_6H_5)_2O$, is formed when phenol is heated with $ZnCl_2$ or $AlCl_3$, but not with H_2SO_4. It crystallizes in needles, and is not decomposed by hydriodic acid. The alkali metals decompose aromatic ethers (B. 1923, 176) *e.g.* $R\cdot O\cdot R' + 2K \rightarrow RK + R'OK$.

Esters.—Phenyl hydrogen sulphate, $C_6H_5\cdot O\cdot SO_2\cdot OH$ (cf. Ethyl hydrogen sulphate), is only capable of existence in the form of salts, being immediately hydrolysed into phenol and sulphuric acid when attempts are made to isolate it. The **potassium** salt $C_6H_5O\cdot SO_2\cdot OK$ (plates, sparingly soluble in

water), is found in the urine of the herbivora and also in human urine after the consumption of phenol, and it may be prepared synthetically by heating potassium phenate with potassium pyro-sulphate in aqueous solution (*Baumann*). It is very stable towards alkalis, but is saponified by hydrochloric acid.

Phenyl acetate, $C_6H_5O \cdot CO \cdot CH_3$, obtained from phenol, acetic anhydride, and dry sodium acetate, is a liquid which boils at 193°, and is readily hydrolysed (cf. Ethyl acetate).

Thio-phenol, *Phenyl hydrosulphide*, $C_6H_5 \cdot SH$, is prepared from benzene-sulphonic chloride, $C_6H_5 \cdot SO_2Cl$, as given at p. 434, or by heating phenol with P_2S_5. It is a liquid of most unpleasant odour and of pronounced mercaptan character (see p. 92). It yields, for instance, a mercury compound, $(C_6H_5S)_2Hg$, crystallizing in glistening needles, and also salts with other metals. When warmed with concentrated H_2SO_4, a cherry-red and then a blue coloration is produced.

Closely related to the above are: (*a*) **phenyl sulphide**, $(C_6H_5)_2S$, which is formed by the action of benzene-diazonium chloride upon thio-phenol (B. **23**, 2469):



$$C_6H_5 \cdot N{:}N \cdot Cl + H \cdot S \cdot C_6H_5 = C_6H_5 \cdot S \cdot C_6H_5 + N_2 + HCl.$$

It is a liquid smelling of leeks, and is oxidizable to **phenyl sulphone**, $(C_6H_5)_2SO_2$; (*b*) **phenyl disulphide**, $(C_6H_5)_2S_2$ (glistening needles, m.-pt. 60°), which is very easily prepared by the action of iodine upon the potassium compound of thio-phenol, or by exposing an ammoniacal solution of the latter to the air. It is readily reduced to thio-phenol, and may be indirectly oxidized to **benzene-disulphoxide**, $(C_6H_5)_2S_2O_2$. (Cf. the corresponding compounds of the fatty series, p. 92, *et seq.*)

SUBSTITUTED PHENOLS

Chloro- and Bromo-phenols.—When chlorine is led into phenol, *o*- and *p*-**chloro-phenols** are formed. These, and also the *m*-compound, may be obtained by reducing and diazotizing the halogenated nitro-benzenes.

Of the isomeric di-derivatives, the *p*-compounds have the highest melting-point and the *o*- the lowest; thus *o*-chloro- and bromo-phenols are liquid and the *p*-compounds solid. When fused with caustic potash they yield dihydroxy-benzenes (p. 440), often with a molecular rearrangement. The chloro-

phenols have a sharp, persistent odour. All the 5 hydrogen atoms of phenol can be replaced by chlorine and bromine.

When an excess of bromine water is added to an aqueous solution of phenol, a precipitate of *s*-**tribromo-phenol** (colourless needles, melting at 92°) is obtained.

Nitroso-phenol, $OH \cdot C_6H_4 \cdot NO$, prepared from phenol and nitrous acid (*Baeyer*, B. 7, 964), by boiling nitroso-dimethylaniline with caustic-soda solution (see p. 406), and by the action of hydroxylamine upon quinone, is identical with quinone monoxime, $O:C_6H_4:N \cdot OH$ (p. 461). It crystallizes in fine colourless needles which readily become brown, or in large greenish-brown plates, and detonates when heated.

Nitro-phenols.—A mixture of *o*- and *p*-**nitro**-phenols is obtained when phenol is mixed with cold dilute nitric acid; the *p*-compound preponderates if the liquid is cold, and the ortho- if it is warm. When distilled with steam, the 1:2 compound volatilizes, while the 1:4 remains behind. *m*-**Nitro-phenol** is obtained by diazotizing *m*-nitraniline.

The *o*- and *p*-compounds can also be obtained by fusing *o*- and *p*-nitranilines with potash, and *p*-nitro-phenol has been synthesised from nitro-malonaldehyde, $NO_2 \cdot CH(CHO)_2$, and acetone (*Hill* and *Torray*, B. 1895, 28, 2598).

The *o*-compound crystallizes in yellow prisms, and melts at 45°, the *m*- in yellow crystals, melting at 96°, and the para- in colourless needles, melting at 114°.

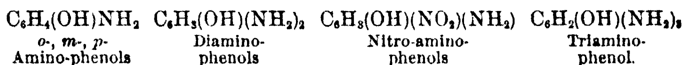
The acid character of phenol is so strengthened by the entrance of the nitro-group that its salts are not decomposed by carbonic acid, but are formed from the nitro-phenols and alkali carbonate. **Sodium** *o*-**nitro-phenate**, $C_6H_4(NO_2)ONa$, crystallizes in dark-red prisms, and **potassium** *p*-**nitro-phenate** in golden needles. (For constitution of the salts, see Chap. XLVII, Absorption Spectra.) Halogens and nitric acid readily substitute further in these mono-nitro-compounds; nitric acid yields two isomeric **dinitro-phenols**, $C_6H_3(NO_2)_2OH$, ($OH:NO_2:NO_2$ = 1:2:4 and 1:2:6, *i.e.* the two NO_2 groups are always in the *m*-position to one another). Further nitration in the presence of sulphuric acid gives—

Picric acid, *s-Trinitro-phenol*, $C_6H_2(NO_2)_3 \cdot OH$, ($OH:NO_2:NO_2:NO_2$ = 1:2:4:6). This compound was discovered in 1799. It may also be prepared by the direct oxidation of *s*-trinitro-benzene with $K_3FeC_6N_6$, and is produced by the action of concentrated nitric acid upon the most varied organic substances, *e.g.* silk, leather, wool, resins, and aniline.

It is a strong acid and forms beautifully crystalline salts, which explode violently when heated or struck. It crystallizes from alcohol or water in yellow plates or prisms, melting at 122°, is only sparingly soluble in water, and the aqueous solutions have a persistent deep-yellow colour. It is used for the preparation of explosives, and is also a yellow dye.

Picryl chloride, $C_6H_2(NO_2)_3Cl$ (from picric acid and PCl_5), resembles the acid chlorides (p. 390) in behaviour. Picric acid forms beautifully crystallizing additive compounds with many aromatic hydrocarbons, and also with amines and phenols.

Amino-phenols are obtained by the reduction of nitrophenols:



$C_6H_4(OH)NH_2$	$C_6H_3(OH)(NH_2)_2$	$C_6H_3(OH)(NO_2)(NH_2)$	$C_6H_2(OH)(NH_2)_3$
o-, *m*-, *p*- Amino-phenols	Diamino- phenols	Nitro-amino- phenols	Triamino- phenol.

In the amino-phenols (*Hofmann*, 1857) the acid character of the phenols is neutralized by the presence of the amino-group, so that they only yield salts with acids. The amino-phenols themselves are relatively unstable, and readily decompose on exposure to moist air or sunlight, but the hydrochlorides are much more stable. Derivatives of these compounds, as phenols and as amines, are known. The amino-hydrogen is readily replaceable by acyl groups.

p-**Amino-phenol**, m.-pt. 184°, obtained by the electrolysis of nitrobenzene in concentrated sulphuric acid (*Gattermann*), or by molecular rearrangement from *β*-phenyl-hydroxylamine, or by passing $p\text{-}OH \cdot C_6H_4 \cdot NO_2 + H_2$ over Cu deposited on pumice and heated at 265° (J. A. C. S. 1919, **41**, 436), is easily oxidized to quinone, $C_6H_4O_2$, and is converted by bleaching-powder into quinone chlor-imide, $O:C_6H_4:NCl$. It is used as a photographic developer under the name of *rodinal*. *Amidol* is a salt of 2 : 4-diamino-phenol, and *metol* is N-methyl-*p*-amino-phenol sulphate and is readily prepared from quinol and methylamine (J. A. C. S. 1919, **41**, 270).

m-**Amino-phenol** and **diethyl**-*m*-**amino-phenol**, $C_6H_4(OH)[N(C_2H_5)_2]$, are formed when *m*-amino-benzene-sulphonic acid or its diethyl-derivative is fused with alkali.

The **anisidines**, *amino-anisoles*, *methoxy-anilines*, $CH_3O \cdot C_6H_4 \cdot NH_2$, and the **phenetidines**, $C_2H_5O \cdot C_6H_4 \cdot NH_2$, are bases similar to aniline, and are used in the colour industry (azo-dyes). **Aceto**-*p*-**phenetidine**, $C_2H_5O \cdot C_6H_4 \cdot NH \cdot CO \cdot CH_3$, *phenacetine* which forms colourless crystals, is a common anti-pyretic.

Diazo-phenols exist in the form of anhydrides, probably $C_6H_4<{O \atop N:N}>$ (*Morgan* and *Porter*, J. C. S. 1915, **107**, 645; cf. *Bamberger*, B. 1915, **48**, 1354). The *m*-compounds do not appear to form such anhydrides (J. C. S. 1917, **111**, 497).

Phenol-sulphonic acids, $OH \cdot C_6H_4 \cdot SO_2 \cdot OH$.—The *o*- and *p*-acids are obtained from phenol and concentrated H_2SO_4 at a moderate temperature, that is, with much greater ease than the benzene-sulphonic acids; the ortho-acid changes into the para- when its aqueous solution is heated. The two acids may be separated by means of their potassium salts. The *m*-compound can be prepared indirectly by fusing *m*-benzene-disulphonic acid with potash. All three are crystalline.

The *o*- and *m*-acids yield *o*- and *m* dihydroxy-benzenes when fused with KOH, but the *p*-acid does not react in this way, being attacked only at temperatures over 320°, when complex products are formed. *o*-Phenol-sulphonic acid is used as an antiseptic under the name of "Aseptol" or "*Sozolic acid*"; similarly, the salts of **di-iodo-*p*-phenol-sulphonic acid**, $OH \cdot C_6H_2I_2 \cdot SO_3H$, "*Sozo-iodol*", form antiseptics resembling iodoform.

HOMOLOGUES OF PHENOL

The homologues of phenol resemble the latter very closely in most of their properties, form perfectly analogous derivatives, possess disinfecting properties, and also a peculiar odour.

They differ from phenol mainly by the presence of side chains which, as in the case of toluene, &c., may undergo certain transformations. Especially when they are used in the form of alkyl or acyl derivatives or acid sulphates, they can be oxidized in such a manner that the side chains (methyl groups) are transformed into carboxyl, with the production of hydroxy-carboxylic acids. The cresols themselves cannot be oxidized in this way even by chromic acid mixture, and are completely destroyed by potassium permanganate. Negative substituents, especially if they are present in the *o*-position, render such oxidation more difficult in acid, but facilitate it in alkaline solution.

All three **cresols**, $CH_3 \cdot C_6H_4 \cdot OH$, are present in coal-tar, and are also contained in the tar from pine and beech wood; they are most readily prepared from the corresponding toluidines.

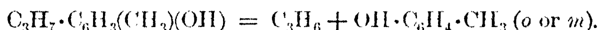
m-**Cresol** is conveniently prepared by heating thymol with phosphoric anhydride and then with potash.

p-**Cresol** is produced during the putrefaction of albumen. Its dinitro-compound is a golden-yellow dye which is used as ammonium or potassium salt under the name **Victoria orange.** Crude cresol is rendered soluble in water by the addition of resin soap or of oil soap; the preparations so obtained are termed *creoline* and *lysol*, and are employed as antiseptics.

Thymol, $C_{10}H_{14}O$, *1-methyl-4-isopropyl-3-hydroxy-benzene*, an important antiseptic, is found together with cymene, $C_{10}H_{14}$, and terpenes, $C_{10}H_{16}$, in oil of thyme, *Thymus Serpyllum*, and the oil from Ajwan fruit, *Carum copticum.*

The isomeric **carvacrol**, *1-methyl-4-isopropyl-2-hydroxy-benzene*, present in *Origanum hirtum*, is prepared either by heating camphor with iodine or from its isomer, carvol, and glacial phosphoric acid.

The *constitutions* of these two phenols have been established as follows: (*a*) Both yield cymene (*p*-methyl-isopropyl-benzene) when heated with phosphorus sulphide and similar compounds. (*b*) Carvacrol, when heated with phosphorus pentoxide, yields propylene and *o*-cresol. (*c*) Thymol, when similarly treated, yields propylene and *m*-cresol.



$$C_3H_7 \cdot C_6H_3(CH_3)(OH) = C_3H_6 + OH \cdot C_6H_4 \cdot CH_3 \; (o \text{ or } m).$$

Eugenol is the chief constituent of oil of cloves and cinnamon leaf oil and is used for manufacturing vanillin (p. 459).

B. Dihydric Phenols

These are analogous to the monohydric compounds in most of their relations, but differ from them in the same way as the dihydric alcohols from the monohydric. The methods of formation are analogous to those used for the monohydric phenols, especially by fusion of sulphonic acids and halogen derivatives with potash; instead, however, of the compound expected, an isomeride which is stable at that high temperature frequently results (see Resorcinol). The *p*-dihydroxy-compounds are characterized by their close connection with the quinones. Many of the polyhydric phenols are strong reducing agents.

Catechol, formerly called **pyrocatechin**, $C_6H_4(OH)_2$ (1:2), which was first obtained by the distillation of **catechin** (*Mimosa Catechu*), is present in raw beet-sugar, and is obtained when many resins or *o*-phenol-sulphonic acid are fused with potash It crystallizes in short, white, rhombic prisms.

which can be sublimed, and dissolves readily in water, alcohol, and ether.

It is usually prepared by heating its mono-methyl ether, **guaiacol**, $C_6H_4(OH)(OCH_3)$, a constituent of beech-wood tar, with hydriodic acid (see Anisole, p. 441). Like most of the polyhydric phenols, it is very unstable in alkaline solution, which quickly becomes green and then black in the air. The aqueous solution is coloured green by ferric chloride, and then violet by ammonia (reactions of the *o*-dihydroxy-compounds). It possesses reducing properties, and precipitates silver even from a cold solution of silver nitrate. By the continued action of chlorine upon it, derivatives of pentamethylene and finally of the fatty series result (*Zincke* and *Kuster*). By boiling it with potash and potassium methyl-sulphate, it may be reconverted into guaiacol, which likewise shows the ferric chloride reaction and possesses reducing powers.

Resorcinol, or *m-Dihydroxy-benzene* (*Hlasiwetz*, *Barth*, 1864), is obtained when many resins (Galbanum, Asafœtida), *m*-phenol-sulphonic acid, all three bromo-benzene-sulphonic acids, or *m*- and *p*-benzene-disulphonic acids are fused with potash. The last-mentioned compounds are employed for its preparation on the technical scale. It crystallizes in rhombic prisms or plates, which quickly become brown in the air, dissolves readily in water, alcohol, and ether, and reduces an aqueous solution of silver nitrate when warmed with it, and an alkaline solution even in the cold. With ferric chloride it gives a dark-violet coloration. It acts therapeutically like carbolic acid, only more mildly.

When heated with phthalic anhydride, it is converted into fluorescein (p. 525); test for *m*-dihydroxy-benzenes), and it is therefore manufactured on the large scale. Nitrous acid or diazonium compounds transform it into azo-dyes; compare Chap. LV, Azo-dyes. Its trinitro-derivative is **styphnic acid**, $C_6H(OH)_2(NO_2)_3$, which is formed by the action of nitric acid upon many gum resins.

Quinol, formerly called **hydroquinone**, *p-dihydroxy-benzene* (*Wohler*, 1844), may be obtained by the oxidation of quinic acid, $C_7H_{12}O_6$, by means of PbO_2, by the hydrolysis of the glucoside arbutin, and from succinylo-succinic ester (cf. p. 371), &c. It is usually prepared by the reduction of quinone with sulphurous acid, and hence the name hydroquinone. It crystallizes in monoclinic plates or hexagonal prisms, of about the same solubility as its isomers, and may be

sublimed. Ammonia colours it reddish-brown, while chromic acid, ferric chloride, and other oxidizing agents convert it into quinone or quinhydrone (p. 460). It melts at 169°, and, being a strong reducing agent, it is used as a developer in photography.

Lead acetate solution yields a white precipitate with a solution of catechol, but none with resorcinol, while quinol is only precipitated in presence of ammonia.

Orcinol, or *m-Dihydroxytoluene*, (CH_3:OH:OH = 1:3:5), is found in many lichens (*Roccella tinctoria*, *Lecanora*, &c.). It is formed by the elimination of carbon dioxide from orsellinic acid, *e.g.* upon fusing extract of aloes with potash, and it can also be prepared synthetically from toluene (B. **15**, 2992). Of especial interest is its synthesis from ethyl acetone-dicarboxylate (p. 270) and sodium (B. **19**, 1446; cf. also *Ingold*, J. C. S. 1922, 1143). It does not yield a fluorescein with phthalic anhydride

Homo-catechol, $C_6H_3(CH_3)(OH)_2$, (CH_3:OH:OH = 1:3:4), deserves mention on account of its mono-methyl ether **creosol**, $CH_3 \cdot C_6H_3(OH)(O \cdot CH_3)$, occurring in beech-wood tar. Creosol is a liquid similar to guaiacol, boiling at 220°, and, as a derivative of catechol, gives a green coloration with ferric chloride.

Quinitol (*Cyclohexane-1:4 diol*), *p-dihydroxy-hexamethylene*, $C_6H_{10}(OH)_2$, a dihydroxy-derivative of reduced benzene, is obtained synthetically by the reduction of *p*-diketo hexamethylene. It crystallizes in crusts, and has a sweet taste with a bitter after-taste; m.-pt. 144°. It is the simplest representative of the inosite sugar group (p. 450).

C. Trihydric Phenols

Pyrogallol, *Pyrogallic acid* (*Scheele*, 1786), 1:2:3-*trihydroxybenzene*, is the most important of these three isomers. It is obtained, apart from synthetical reactions, by heating gallic acid, when carbon dioxide is eliminated: $C_6H_2(OH)_3 \cdot CO_2H = C_6H_3(OH)_3 + CO_2$. It crystallizes in white plates, melts at 132°, is readily soluble in water, and capable of subliming without decomposition. It is an energetic reducing agent, *e.g.* for silver salts, and is used as a developer in photography. Its alkaline solution rapidly absorbs oxygen, hence its use in gas analysis.

In the presence of NaOH the oxidation product appears to be a hexa-hydroxy-triphenoquinone, $O:C_6H_2(OH)_2:C_6H_2(OH)_2:C_6H_2(OH)_2:O$ (J. C. S. 1915, **107**, 1217), or in the presence of $Ba(OH)_2$ 2:3:4:2′:3′:4′-hexa-hydroxy-diphenyl, $(OH)_3C_6H_2 \cdot C_6H_2(OH)_3$ (A. 1912, **394**, 249).

The aqueous solution is coloured bluish-black by a solution of ferrous sulphate containing ferric salt, and purple-red by iodine. It does not react with hydroxylamine (cf. Phloroglucinol).

Pyrogallol dimethyl ether, $C_6H_3(OH)(OCH_3)_2$ (*Hofmann*), is contained in beech-wood tar, as are likewise the dimethyl ethers of the compounds $C_6H_2(CH_3)(OH)_3$ and $C_6H_2(C_3H_7)(OH)_3$, homologous with pyrogallol.

Phloroglucinol, or 1:3:5-*Trihydroxy-benzene* (*Hlasiwetz*, 1855), is obtained by the fusion of various resins and of resorcinol with potash or soda, by the action of alkali upon the glucoside phloretin, and by fusing its dicarboxylic ester (whose synthetical formation is given on p. 470) with potash. It forms large prisms which weather in the air, melts at 218°, and sublimes without decomposition. With ferric chloride it gives a dark-violet coloration, its solutions in alkalis readily absorb carbon dioxide, and it possesses reducing properties.

Phloroglucinol is a typical example of a tautomeric compound.

In many reactions, *e.g.* (*a*) the formation of metallic derivatives, $C_6H_3(OK)_3$; of a trimethyl ether, $C_6H_3(OCH_3)$, which is insoluble in alkali; and of a triacetyl derivative, $C_6H_3(OAc)_3$; (*b*) its combination with phenyl-carbimide to form a tricarbaniline derivative, $C_6H_3(O \cdot CO \cdot NH \cdot C_6H_5)_3$, it reacts as a normal phenol, *i.e.* as sym. trihydroxy-benzene. On the other hand, however, in certain of its reactions it behaves as a ketone, *i.e.* as triketo-hexamethylene, $CO<\begin{matrix}CH_2 \cdot CO\\CH_2 \cdot CO\end{matrix}>CH_2$; thus it yields a trioxime, $C_6H_6(:N \cdot OH)_3$, and when alkylated in presence of alcoholic potash yields tetra- and hexa-alkyl derivatives, *e.g.* $C_6Me_6O_3$, $CO<\begin{matrix}CMe_2 \cdot CO\\CMe_2 \cdot CO\end{matrix}>CMe_2$. Its ultra-violet absorption spectrum (*Hedley*, J. C. S. 1906, 730) resembles that of other phenols.

Hydroxy-quinol, 1:2:4-*Trihydroxy-benzene*, is obtained by fusing quinol with potash. Like pyrogallol, it yields no oxime with hydroxylamine.

Hexahydroxy-benzene, $C_6(OH)_6$, forms as its potassium salt potassium carboxide, $C_6O_6K_6$, the explosive compound sometimes obtained in the manufacture of metallic potassium. It crystallizes in colourless prisms, has no definite melting-point, but decomposes at about 200°, and can be converted into its quinone.

Quercitol, $C_6H_7(OH)_5$, found in the oak, and **inosite or inositol,** $C_6H_6(OH)_6$, found in the muscles of the heart, are polyhydroxy-derivatives of hexamethylene. In many respects they closely resemble the aliphatic polyhydric alcohols rhamnitol and sorbitol. Quercitol melts at 235°, is optically active, and has $[\alpha]_D = +24{\cdot}16$. Inositol or hexahydroxy-cyclohexane exists in an inactive and in *d*-, *l*-, and *r*-modifications.

XXV. AROMATIC ALCOHOLS, ALDEHYDES, AND KETONES

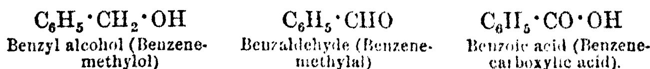
A. Aromatic Alcohols

While the phenols remind us of the tertiary alcohols of the fatty series, although they differ from these in many points, we are acquainted with compounds which possess the alcoholic character in its entirety; they are termed aromatic alcohols. The simplest and most important of these is (primary) benzyl alcohol, $C_7H_7{\cdot}OH$, which is isomeric with the cresols.



Characteristic of all aromatic alcohols is the fact that the hydroxyl group is attached to a carbon atom of a side chain and not to a carbon atom of the nucleus. It is thus clear that each alcohol will have one or more phenols isomeric with it. The three cresols, *o*-, *m*-, *p*-methylphenols are isomeric with benzyl alcohol and *β*-phenylethyl alcohol is isomeric with the dimethylphenols and with the ethylphenols. The alcohols are also isomeric with the phenolic ethers, *e.g.* benzyl alcohol with phenyl methyl ether.

The formula, $C_6H_5{\cdot}CH_2{\cdot}OH$, for benzyl alcohol follows from the formation of the alcohol from benzyl chloride, $C_6H_5{\cdot}CH_2Cl$ (and *vice versa*), and also from the fact that it can be oxidized to an aldehyde and an acid containing the same number of carbon atoms in the molecule as itself, these being likewise mono-derivatives of benzene:



Benzyl alcohol may also be looked upon as methyl alcohol

in which one atom of hydrogen is replaced by the group C_6H_5:


$H\cdot CH_2\cdot OH$ (carbinol) $C_6H_5\cdot CH_2\cdot OH$ (phenyl-carbinol)

and is therefore the simplest aromatic alcohol.

As in the fatty series, so in the aromatic, the alcohols can be classified into the three main groups: primary, secondary, and tertiary. The primary contain the group $-CH_2\cdot OH$, the secondary the group $=CH\cdot OH$, and the tertiary the group $\equiv C\cdot OH$, and all must have at least one aryl group attached to the characteristic group. In triphylcarbinol, $(C_6H_5)_3C\cdot OH$, all three alkyl groups are aromatic, but this is not essential, *e.g.* phenyldimethylcarbinol, $C_6H_5\cdot C(CH_3)_2\cdot OH$ is a tertiary aromatic alcohol.

The primary, secondary, and tertiary are differentiated in exactly the same manner as the corresponding groups in the aliphatic series. Thus the primary yield on oxidation first aldehydes and then acids containing the same number of carbon atoms, the secondary yield ketones, *e.g.* $(C_6H_5)_2CH\cdot OH$ yields $(C_6H_5)_2CO$, benzophenone, and the tertiary are not readily oxidized.

Of the polyhydric alcohols, phenyl-glycerol (1-phenyl-1:2:3-trihydroxypropane) is the most important. All of these contain the hydroxyl radicals attached to carbon atoms of the side chain and not to those of the nucleus, and this is the fundamental difference between an aromatic alcohol and a phenol. The alcohols are not of the same commercial importance as the phenols, and hence have not been investigated to the same extent.

Only a few occur naturally, *e.g.* β-phenylethyl alcohol; they are usually prepared by laboratory methods, *e.g.* the primary by the reduction of the esters of aromatic acids by *Bouveault's* method, or of the acid amides; the secondary by the reduction of ketones or by the aid of *Grignard's* reagents and the latter by the same method from esters or ketones (p. 384).

All these compounds are, as alcohols, perfectly analogous to the alcohols of the fatty series, so far as regards the formation of alcoholates, ethers, esters, mercaptans, amines, phosphines, &c. They are, however, at the same time benzene derivatives, and consequently yield chloro-, bromo-, nitro-, amino-, &c., substitution products. Unsaturated aromatic alcohols are also known, which resemble the unsaturated compounds of

the fatty series to the closest extent in their chemical behaviour, but are at the same time benzene derivatives.

Benzyl alcohol, $C_6H_5 \cdot CH_2 \cdot OH$, is a colourless liquid of faint aromatic odour, sparingly soluble in water, and boils at 204°. It occurs naturally in Peru and Tolu balsams as benzoic and cinnamic esters, and is formed from benzyl chloride just as alcohol is from ethyl chloride. It is usually prepared by the action of concentrated aqueous potash on benzaldehyde, whereby the one half of the aldehyde is oxidized and the remainder reduced (B. **14**, 2394):



$$2C_6H_5 \cdot CHO + KOH = C_6H_5 \cdot CH_2 \cdot OH + C_6H_5 \cdot COOK.$$

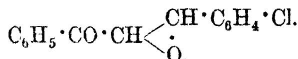
Benzyl alcohol is also formed when benzamide is reduced with sodium amalgam. This is a reaction which has been employed for the preparation of a number of substituted benzyl alcohols (*Hutchinson*, B. 1891, **24**, 173).

Phenyl-ethyl alcohol, $C_6H_5 \cdot CH_2 \cdot CH_2 \cdot OH$, b.-pt. 220°, is prepared by reducing ethyl phenylacetate with sodium and alcohol. It is an important constituent of rose oil and of many blended perfumes.

Phenyl-methyl-carbinol, $C_6H_5 \cdot CH(OH) \cdot CH_3$, b.-pt. 203°, can be prepared by reducing acetophenone, $C_6H_5 \cdot CO \cdot CH_3$ (p. 457), into which it is reconverted by gentle oxidation.

The simplest of the unsaturated alcohols is **cinnamic alcohol,** $C_6H_5 \cdot CH:CH \cdot CH_2OH$, which occurs as cinnamic ester ("styracin") in storax. It crystallizes in glistening needles of hyacinth-like odour, yields cinnamic acid when gently oxidized, and benzoic when the oxidation is more vigorous.

Ethylene oxides containing aryl substituents are much more stable than those containing alphyl-groups (p. 201). Thus *w*-bromoacetophenone, $C_6H_5 \cdot CO \cdot CH_2Br$, readily condenses in the presence of NaOEt with substituted benzaldehydes containing negative groups, yielding **ethylene oxides** of the type,



$$C_6H_5 \cdot CO \cdot CH \langle \begin{matrix} CH \cdot C_6H_4 \cdot Cl. \\ \vdots \\ O. \end{matrix}$$

Cf. B. 1917, **50**, 1457, and 1918, **51**, 192.

B. Aromatic Aldehydes

Benzaldehyde, *Benzene-methylal*, or *oil of bitter almonds*, $C_6H_5 \cdot CHO$, was discovered in 1803 and investigated by *Liebig* and *Wöhler* (A. **22**, 1). It is a colourless, strongly refracting

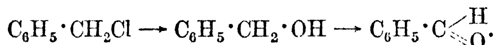
liquid of agreeable bitter almond-oil odour. It boils at 179°, has a sp. gr. 1·05 at 15°, and is readily soluble in alcohol and ether, but only sparingly in water (1 in 30).

Many of the modes of formation are analogous to those described under the aliphatic aldehydes (pp. 129 and 130):

(*a*) By the oxidation of the corresponding alcohol. This reaction is of little practical value, as the alcohols themselves are usually prepared from the aldehydes.

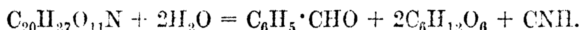
(*b*) By the distillation of the calcium salt of the corresponding acid, benzoic acid, with calcium formate.

(*c*) By heating the corresponding dichloride, benzal chloride, or benzylidene chloride, $C_6H_5 \cdot CHCl_2$ (from toluene), with water or sulphuric acid, or, as is done on the technical scale, with water and lime; also by heating benzyl chloride, $C_6H_5 \cdot CH_2Cl$, with water and plumbous or cupric nitrate, or the bromide with sodium nitrate (U. S. P.), or by oxidizing the chloride with sodium dichromate and caustic soda (E. P.). This method involves processes of hydrolysis and oxidation:



$$C_6H_5 \cdot CH_2Cl \rightarrow C_6H_5 \cdot CH_2 \cdot OH \rightarrow C_6H_5 \cdot C \begin{smallmatrix} \diagup H \\ \diagdown O \end{smallmatrix}.$$

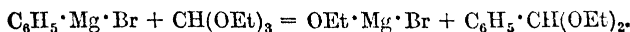
(*d*) Together with dextrose and hydrocyanic acid by decomposing **amygdalin**, $C_{20}H_{27}O_{11}N$, a glucoside (see Glucosides) which occurs in bitter almonds and crystallizes in white plates, either by means of sulphuric acid or by emulsin (an enzyme likewise present in bitter almonds (p. 276 and Chap. XLVIII)):



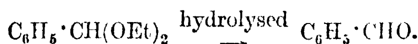
$$C_{20}H_{27}O_{11}N + 2H_2O = C_6H_5 \cdot CHO + 2C_6H_{12}O_6 + CNH.$$

(*e*) By the action of chromyl chloride, CrO_2Cl_2, upon toluene. This is *Etard's* reaction, and is of great value for the synthesis of aldehydes and also of certain ketones from hydrocarbons. An additive compound, $C_6H_5 \cdot CH_3(CrO_2Cl_2)_2$, is first formed, and yields the aldehyde on the addition of water (B. **17**, 1462, 1700; **32**, 1050).

(*f*) By the action of *Grignard's* phenyl-magnesium bromide on ethyl orthoformate (*Bodroux*, C. R. 1904, **138**, 92 and 700), *e.g.*:



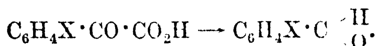
$$C_6H_5 \cdot Mg \cdot Br + CH(OEt)_3 = OEt \cdot Mg \cdot Br + C_6H_5 \cdot CH(OEt)_2.$$



$$C_6H_5 \cdot CH(OEt)_2 \xrightarrow{\text{hydrolysed}} C_6H_5 \cdot CHO.$$

Gattermann and *Maffezzoli* (B. 1903, **36**, 4152) have used *Grignard's* compound with a large excess of ethyl formate at low temperatures.*

(*g*) Homologues of benzaldehyde are sometimes prepared by the elimination of carbon dioxide from substituted phenyl-glyoxylic acids by a process of distillation:



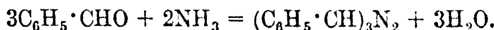
$$C_6H_4X\cdot CO\cdot CO_2H \rightarrow C_6H_4X\cdot C\genfrac{}{}{0pt}{}{H}{O}.$$

(*h*) A simple synthesis can be effected by heating the hydrocarbon with carbon monoxide under a pressure of 50–90 atmospheres (E. P. 1915).

(*i*) By passing hydrogen into a boiling 20-per-cent solution of benzoyl chloride in xylene, using palladinized $BaSO_4$ as catalyst, cf. p. 186.

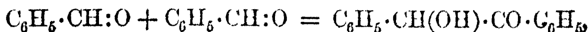
Behaviour.—1. Its behaviour is that of an aldehyde, and in many respects it closely resembles the aliphatic aldehydes. Thus it is (*a*) easily oxidizable to the acid, and on this account reduces an ammoniacal silver solution with the production of a mirror; (*b*) reducible to the alcohol; (*c*) capable of forming a crystalline additive compound with $NaHSO_3$; (*d*) capable of combining with HCN (see Mandelic acid); (*e*) capable of reacting with hydroxylamine and phenyl-hydrazine to benzaldoxime, $C_6H_5\cdot CH:N\cdot OH$, and benzaldehyde-phenyl-hydrazone, $C_6H_5\cdot CH:N_2H\cdot C_6H_5$, respectively; (*f*) converted into benzylidene chloride, $C_6H_5\cdot CHCl_2$, by the action of PCl_5.

2. Benzaldehyde does not form an additive compound with ammonia analogous to the aldehyde-ammonias of the aliphatic series, but enters into a somewhat complex condensation, yielding hydrobenzamide:



$$3C_6H_5\cdot CHO + 2NH_3 = (C_6H_5\cdot CH)_3N_2 + 3H_2O.$$

3. Benzaldehyde and its homologues can undergo polymerization, *e.g.* when an alcoholic solution of benzaldehyde is boiled with potassium cyanide, **benzoin** is formed (a balanced reaction, J. A. C. S. 1923, 836):



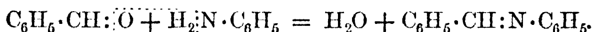
$$C_6H_5\cdot CH:O + C_6H_5\cdot CH:O = C_6H_5\cdot CH(OH)\cdot CO\cdot C_6H_5,$$

a compound which is both a secondary alcohol and a ketone.

* For synthetical methods see *Gattermann*, A. 1906, **347**, 347.

4. A number of condensation products can be obtained from the aromatic aldehydes, and many of these are of commercial importance. The condensation usually takes place in the presence of a condensing agent, *e.g.* acetic anhydride, anhydrous zinc chloride, potassium hydroxide, sodium ethoxide, &c. Among some of the simplest of these condensations are:—

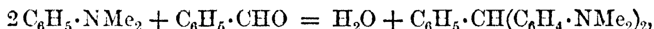
(*a*) With primary amines. The formation of benzylidene anilines (*Schiff's Bases*):



$$C_6H_5\cdot CH:O + H_2:N\cdot C_6H_5 = H_2O + C_6H_5\cdot CH:N\cdot C_6H_5.$$

It has been shown recently that this reaction is preceded by the formation of an additive compound, $C_6H_5\cdot CH(OH)\cdot NH\cdot C_6H_5$, which then passes into the benzylidene derivative. A few such additive compounds have actually been isolated. (*Dimroth* and *Zoeppritz*, B. 1902, **35**, 984.)

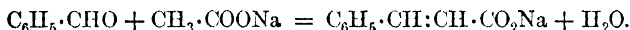
(*b*) With tertiary amines, *e.g.*:



$$2\,C_6H_5\cdot NMe_2 + C_6H_5\cdot CHO = H_2O + C_6H_5\cdot CH(C_6H_4\cdot NMe_2)_2,$$

when a substituted diamino-derivative of triphenyl-methane is produced (Chap. XXX, 1).

(*c*) With the sodium salts of fatty acids, when unsaturated acids are formed (*Perkin's Synthesis*, Chap. XXVI, A.):



$$C_6H_5\cdot CHO + CH_3\cdot COONa = C_6H_5\cdot CH:CH\cdot CO_2Na + H_2O.$$

(*d*) With fatty aldehydes, ketones, &c., when unsaturated aldehydes (*e.g.* cinnamic aldehyde) or ketones are formed:



$$C_6H_5\cdot CH:O + CH_3\cdot CH:O = H_2O + C_6H_5\cdot CH:CH\cdot CHO.$$

5. Its reaction with alkalis (p. 452) is also different; in the fatty series aldehyde resins are formed, and with benzaldehyde a mixture of primary alcohol and the corresponding acid. This latter reaction is characteristic of aldehydes in which the CHO group is directly attached to the benzene nucleus.

6. As a benzene derivative, it can be substituted by halogens (indirectly), and can be nitrated, sulphonated, &c. (directly).

As in the case of toluene, chlorine enters the side chain at the boiling temperature, with formation of benzoyl chloride, $C_6H_5\cdot COCl$.

Among its derivatives, the following deserve mention:—

α-Benzaldoxime, *Benz-α-aldoxime*, $C_6H_5\cdot CH:N\cdot OH$, is

formed from benzaldehyde and hydroxylamine; it melts at 35°, and decomposes when boiled. It can be transformed by means of acids into the isomeric **β-benzaldoxime,** which melts at 125° (for velocity, cf. *Patterson,* J. C. S. 1907, 504; 1908, 1041), and in contradistinction to the isomer, readily reacts with acetic anhydride yielding benzonitrile. The oximes are stereo-isomeric (Nitrogen-isomerism). (Cf. Chap. XLVI.)

Benzaldehyde - phenyl - hydrazone, $C_6H_5 \cdot CH:N \cdot NHC_6H_5$, forms colourless crystals, melting at 152°. **Benzylideneazine,** $CHPh:N \cdot N:CHPh$, from benzaldehyde and hydrazine sulphate, has m.-pt. 93°.

Nitro-benzaldehydes, $NO_2 \cdot C_6H_4 \cdot CHO$.—The *m*-compound is the chief product of nitration, but some 20 per cent of the *o*-compound is formed at the same time. The latter is prepared by oxidizing *o*-nitro-cinnamic acid by $KMnO_4$, in presence of benzene; it forms long colourless needles, melting at 46°, yields indigo (Chap. XXXV, C.) with acetone and caustic soda, and on exposure to sunlight forms *o*-nitroso-benzoic acid. It can be reduced to *o*-**amino-benzaldehyde,** $NH_2 \cdot C_6H_4 \cdot CHO$, a compound crystallizing in silvery glistening plates, m.-pt. 46°, which is of value for various synthetical reactions. (See Quinoline; also B. **16,** 1833.) *m*-**Amino-benzaldehyde,** prepared by reducing the bisulphite compound of *m*-nitro-benzaldehyde, is used in the production of triphenyl-methane dyes.

Cinnamic aldehyde, $C_6H_5 \cdot CH:CH \cdot CHO$, is the chief constituent of oil of cinnamon (*Cinnamonum zeylanicum*) of Ceylon, and oil of cassia (*C. cassia*) of China, from which it may be isolated by means of its bisulphite-compound. It is an oil of aromatic odour, boils at 246°, and is readily volatile with steam. In addition to its properties as an aldehyde, it also possesses the properties of an unsaturated compound, *e.g.* forms a dibromide. Its reaction with potassium hydrogen sulphite is characteristic. It first forms an additive compound, $C_6H_5CH:CH \cdot CH(OH)(SO_3K)$, like an ordinary aldehyde, and then, as an unsaturated compound, combines with a second molecule of the sulphite, yielding $C_6H_5 \cdot CH(SO_3K) \cdot CH_2 \cdot CH(OH)(SO_3K) + 2H_2O$. (B. **24,** 1805; **31,** 3301.)

When cinnamic aldehyde is used in many of the condensations mentioned on p. 454 the product contains two olefine linkings, thus with malonic ester the product, $C_6H_5 \cdot CH:CH \cdot CH:C(CO_2Et)_2$, ethyl cinnamylidene-malonate is formed.

C. Aromatic Ketones

The aromatic ketones are usually divided into (1) mixed ketones, aryl- alphyl ketones, *e.g.* $C_6H_5 \cdot CO \cdot CH_3$, and (2) true aromatic or diaryl ketones, *e.g.* $C_6H_5 \cdot CO \cdot C_6H_5$.

Acetophenone, *Phenyl-methyl ketone*, $C_6H_5 \cdot CO \cdot CH_3$, crystallizes in colourless plates, is readily soluble in water, melts at 20°, boils at 200°. It is obtained by the normal modes of preparation for ketones, *e.g.* by distilling a mixture of acetate and benzoate of calcium, as also by the *Friedel-Crafts'* synthesis (p. 374), viz. the conjoint action of acetyl chloride and aluminium chloride upon benzene. Sulphoacetic acid (acetic anhydride and sulphuric acid) can be substituted for the acid chloride and $AlCl_3$, *e.g.* in the case of guaiacol (B. 1922, 1892; J. pr., 1921 [ii], **103**, 329). When benzene and its derivatives are converted into ketones by this method, only one acyl group is introduced as a rule, and this into the para-position with respect to any alkyl group already present. With a sym. trialkylated benzene, *e.g.* mesitylene, it has been found possible to introduce two acyl groups, *e.g.* diacetyl-mesitylene, $(CH_3)_3C_6H(COCH_3)_2$ (*V. Meyer*, B. 1895, **28**, 3212; 1896, **29**, 846, 1413). When the temperature is kept low by diluting the mixture with carbon disulphide, a good yield of ketone may be obtained by the *Friedel-Crafts'* method.

Acetophenone unites in itself the properties of a ketone of the fatty series and of a benzene derivative. It yields benzoic acid and carbon dioxide when oxidized with ordinary oxidizing agents, but with cold alkaline permanganate it yields $C_6H_5 \cdot CO \cdot CO_2H$, **phenyl-glyoxylic acid** or **benzoyl-formic acid.** When warmed with halogens, it is substituted in the side chain (*e.g.* to "**phenacyl bromide**", $C_6H_5 \cdot CO \cdot CH_2Br$), and with nitric acid it is nitrated. It is used as a soporific under the name of "*Hypnone*". Its **oxime** melts at 59°, and its **phenyl-hydrazone** at 105°. It combines with hydrogen cyanide to form the nitrile of α-phenyl-lactic acid, but cannot form an additive compound with sodium hydrogen sulphite.

Its homologues closely resemble it, but are liquid at the ordinary temperature. Acetophenone and some of its homologues can be prepared from hydrocarbons with long side chains by *Etard's* reaction (see p. 453: B. **23**, 1070; **24**, 1356). Aromatic polyketones (cf. p. 229) have also been prepared, *e.g.* **benzoyl-acetone,** $C_6H_5 \cdot CO \cdot CH_2 \cdot CO \cdot CH_3$, and **acetophenone-acetone,** $C_6H_5 \cdot CO \cdot CH_2 \cdot CH_2 \cdot CO \cdot CH_3$. The latter, like

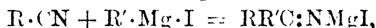
acetonyl-acetone, is readily converted into furane, pyrrole, and thiophene derivatives (Chap. XXXIV).

Benzaldehyde condenses with acetone and acetophenone in the presence of alkalis, yielding unsaturated ketones, *e.g.* **Benzylideneacetone**, $CHPh:CH \cdot CO \cdot CH_3$, m.-pt. 41°, and **benzylideneacetophenone**, *chalcone*, $CHPh \cdot CH:CH \cdot CO \cdot C_6H_5$, m.-pt. 58°.

Benzophenone, *Diphenyl-ketone*, $C_6H_5 \cdot CO \cdot C_6H_5$, may be obtained (1) by distilling calcium benzoate, (2) by the *Friedel-Crafts'* synthesis, (3) by the oxidation of diphenylmethane, $(C_6H_5)_2CH_2$, or of diphenyl-carbinol, $(C_6H_5)_2CH \cdot OH$.

Good yields of ketones are not usually obtained by the action of *Grignard's* reagents on acid chlorides; as a rule the reaction proceeds further, and a tertiary alcohol is obtained (p. 384). An exception is found in the reaction between α-naphthyl-magnesium bromide and benzoyl chloride.

Ketones can (*Blaise*, C. R. 1901, **132**, 38; **133**, 299) be synthesized from *Grignard's* reagents and nitriles, or amides:



$$R \cdot CN + R' \cdot Mg \cdot I = RR'C:NMgI,$$

and this with water gives $R \cdot CO \cdot R' + NH_3 + I \cdot Mg \cdot OH$. Acid amides react in a somewhat similar manner.

Benzophenone is dimorphous; the stable modification melts at 49°, and when boiled or distilled yields the unstable modification, melting at 26°; but this gradually passes back again into the stable modification. The reaction is, however, considerably accelerated by the addition of a minute crystal of the stable compound. It yields an **oxime** melting at 140° and a **phenyl-hydrazone** melting at 105°.

When reduced with zinc dust or hydriodic acid and red phosphorus, it yields diphenylmethane.

D. Hydroxy or Phenolic Alcohols, Aldehydes, and Ketones

Formula.	Name.	Constitution.
$OH \cdot C_6H_4 \cdot CH_2OH$	Saligenin,	*o*-hydroxy-benzyl-alcohol.
$OCH_3 \cdot C_6H_4 \cdot CH_2OH$	Anisyl alcohol,	*p*-methoxy-benzyl alcohol.
$OH \cdot C_6H_3(OMe) \cdot CH_2OH$	Vanil alcohol,	3-methoxy-4-hydroxy-benzyl alcohol.
$OH \cdot C_6H_3(OMe)(C_3H_4 \cdot OH)$	Coniferyl alcohol,	$[OCH_3:OH = 3:4]$.
$OH \cdot C_6H_4 \cdot CHO$	Salicyl-aldehyde,	*o*-hydroxy benzaldehyde.
$OCH_3 \cdot C_6H_4 \cdot CHO$	Anisaldehyde,	*p*-methoxy-benzaldehyde.
$(OH)_2C_6H_3 \cdot CHO$	Procatechuic aldehyde,	3:4-dihydroxy-benzaldehyde,
$OH \cdot C_6H_3(OMe) \cdot CHO$	Vanillin,	3-methoxy-4-hydroxy-benzaldehyde.
$CH_2O_2:C_6H_3 \cdot CHO$	Piperonal,	methylene-protocatechuic aldehyde.

A large number of compounds are known which possess

phenolic properties in addition to those of an alcohol, aldehyde, or ketone. Several of these compounds occur as glucosides in nature. Anisaldehyde is obtained from the oxidation of anisole (methyl phenyl ether).

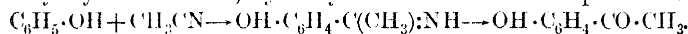
Tiemann-Reimer's synthesis consists in heating a phenol with chloroform in the presence of concentrated KOH:



$$C_6H_5 \cdot OK + CHCl_3 = HCl + CHCl_2 \cdot C_6H_4 \cdot OK,$$

and the dichlor-derivative thus formed is hydrolysed by the alkali to $CHO \cdot C_6H_4 \cdot OK$. The formyl-group $\cdot CH{:}O$ always takes up the *o*- or *p*-position with respect to the hydroxy-group, and, as a rule, the *o*- and *p*-compounds are formed together, and may often be separated by the difference in volatility of the two compounds in steam.

In the *Gattermann* synthesis (B. 1915, **48**, 1112), a phenol is heated with HCN and HCl and subsequently hydrolysed. If an alkyl cyanide is used, hydroxy-ketones are the final products:



$$C_6H_5 \cdot OH + CH_3CN \rightarrow OH \cdot C_6H_4 \cdot C(CH_3){:}NH \rightarrow OH \cdot C_6H_4 \cdot CO \cdot CH_3.$$

An analogous synthesis is passing a rapid current of dry HCl into an ethereal solution of cyanogen bromide and resorcinol or some other polyhydric phenol (*Karrer*, Helv. 1919, **2**, 89).

Vanillin crystallizes in beautiful needles, and is prepared on the large scale from **coniferin**, $C_{16}H_{22}O_8 + 2H_2O$, a compound occurring in the sap of the cambium in the Coniferæ. This is hydrolysed by acids into glucose and **coniferyl alcohol**, $C_6H_3(OH)(OCH_3)(C_3H_4 \cdot OH)$, and the latter yields vanillin when oxidized (*Tiemann* and *Haarmann*); the CH_3 group is removed by heating with hydrochloric acid at 200°, with the formation of protocatechuic aldehyde. Vanillin is also found in vanilla pod, asparagus, beet-sugar, asafœtida, and certain balsams.

Vanillin can also be obtained synthetically from *m*-chloro-*p*-nitro-benzaldehyde (from *m*-chloro-*p*-nitro-toluene), but is usually manufactured from eugenol (p. 437) which is transformed into isoeugenol, $OH \cdot C_6H_3(OMe)CH{:}CH \cdot CH_3$ by alcoholic potash, then acetylated and finally oxidized.

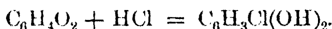
E. Quinones

Quinones are compounds derived from benzene and its derivatives by the replacement of two atoms of hydrogen by two of oxygen, *e.g.* $C_6H_4O_2$. As a group they are characterized by (*a*) their yellow colour, (*b*) being readily reduced to dihydric phenols, and hence often acting as oxidizing agents. They are often divided into **para-quinones** and **ortho-quinones**.

p-Benzoquinone or *Quinone*, $C_6H_4O_2$ (1838), is produced when chromic acid is added to a solution of quinol. It crystallizes in yellow needles or prisms of a characteristic pungent odour something like that of nut-shells, is sparingly soluble in water but readily in alcohol and ether, and can be sublimed; m.-pt. 116°. Corresponding with it we have a large number of higher homologues, &c. These also are solids, mostly of a yellow colour, and are volatile with steam; they are obtained by the oxidation of the corresponding dihydroxy-phenols, or of polyhydric phenols, which contain two hydroxyls in the para-position.

Quinone is also formed by the oxidation of many aniline and phenol derivatives belonging to the para-series, *e.g.* *p*-amino-phenol, sulphanilic acid, and *p*-phenol-sulphonic acid; it is usually prepared by the oxidation of aniline itself by means of chromic acid (see B. 1887, **20**, 2283). It was first obtained by distilling quinic acid with manganese dioxide and sulphuric acid. Exposure to light causes it to turn brown, and it colours the skin yellow-brown. It is readily reduced to quinol by SO_2, HI, $SnCl_2$ and HCl, &c., and can therefore act as an oxidizing agent.

In chloroform solution it takes up two or four atoms of bromine to form a di- or tetra-bromide ($C_6H_4O_2 \cdot Br_4$). Under other conditions chlorine and bromine act upon it as substituents, while hydrochloric acid forms chloroquinol:

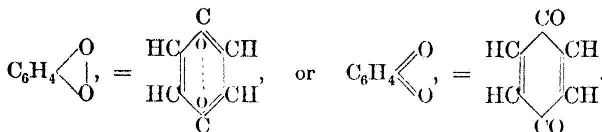


$$C_6H_4O_2 + HCl = C_6H_3Cl(OH)_2.$$

It yields sparingly soluble, coloured crystalline compounds with complex hydrocarbons, phenols, phenolic ethers, and amines (*Pfeiffer*). With quinol it forms an additive compound termed **quinhydrone**, $C_6H_4O_2 + C_6H_4(OH)_2$; this crystallizes in green prisms with a metallic lustre, and is also formed as an intermediate product in the oxidation of quinol or in the reduction of quinone. Its constitution has not been definitely settled. (Cf. *Siegmunds*, J. pr. 1911, **83**, 553; also *Knorr*, B. 1911, **44**, 1503.)

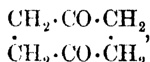
Constitution.—Quinone is derived from benzene by the exchange of two atoms of hydrogen for two of oxygen, which, from the close connection between quinone and quinol, must be in the *p*-position. The constitution of quinone may be explained either by assuming that these two oxygen atoms are linked together, as in peroxide of hydrogen, $H \cdot O \cdot O \cdot H$, so that the benzene nucleus remains unchanged, or that the

latter experiences a partial reduction, with the formation of a derivative of C_6H_8, a "diketo-dihydro-benzene":



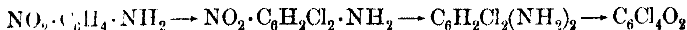
According to the first of these two formulæ, quinone would be a peroxide; according to the second, a ketone. In favour of the latter view (which was brought forward by *Fittig*, and is now almost universally accepted) are (1) the fact that quinone can be converted into an oxime, $C_2H_2 < \begin{matrix} C(N \cdot OH) \\ CO \end{matrix} > C_2H_2$ (identical with nitroso-phenol, p. 143), and into a dioxime, quinone dioxime, $C_2H_2 < \begin{matrix} C(N \cdot OH) \\ C(N \cdot OH) \end{matrix} > C_2H_2$ (B. **20**, 613); (2) its power of forming additive compounds with bromine; and (3) its relations to the analogously constituted anthraquinone. (Cf. B. **18**, 568; A. **223**, 170; J. pr. **42**, 161; also chapter on Physical Properties and Constitution.)

Tetrahydro-quinone, *p-Diketo-hexamethylene* (*cyclo-hexane*-1:4-*dione*),



can be prepared by hydrolysing and eliminating the carboxyl groups from succinylo-succinic ester (p. 371). It crystallizes in colourless prisms, melts at 78°, and, on reduction, yields quinitol (p. 448). (Cf. B. **22**, 2168; **23**, 1272.)

Chloranil, *Tetrachloro-quinone*, $C_6Cl_4O_2$, which crystallizes in lustrous yellow plates, is obtained by chlorinating quinone and also by oxidizing many organic compounds, *e.g.* phenol, with HCl and $KClO_3$. A good yield may be obtained by chlorinating *p*-nitraniline, reducing the 2:6-dichloro-4-nitraniline thus obtained to 2:6-dichloro-*p*-phenylene-diamine, and then oxidizing and chlorinating by means of potassium chlorate and hydrochloric acid:



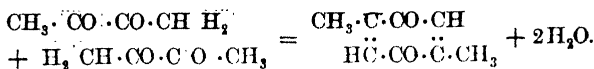
$$NO_2 \cdot C_6H_4 \cdot NH_2 \longrightarrow NO_2 \cdot C_6H_2Cl_2 \cdot NH_2 \longrightarrow C_6H_2Cl_2(NH_2)_2 \longrightarrow C_6Cl_4O_2$$

(*Witt*, Abstr. 1904, **1**, 174.) When reduced, it yields the colourless tetrachloro-quinol; it also acts as an oxidizing agent, converting *e.g.* dimethylaniline into methyl-violet. A dilute

solution of potassium hydroxide transforms it into **potassium chloranilate**, $C_6Cl_2O_2(OK)_2 + H_2O$ (dark-red needles), corresponding with which there is also an analogous nitro-compound, **potassium nitranilate**, $C_6(NO_2)_2O_2(OK)_2$. The latter salt is distinguished by its sparing solubility, hence its formation may be made use of as a test for potassium compounds. (For its constitution, see B. **19**, 2398.)

Chlorine transforms chloranil and chloranilic acid into complex chloro-products of the hexa- and pentamethylene series, and finally into chlorinated fatty compounds. (For a tabular summary, see *Hantzsch*, B. **22**, 2841; cf. also B. 25, 827, 842.)

Toluquinone, $C_6H_3(O_2)(CH_3)$, **xyloquinone**, $C_6H_2(O_2)(CH_3)_2$, **thymoquinone**, $C_6H_2(O_2)(CH_3)(C_3H_7)$, &c., are known. Several of these can be prepared synthetically by the condensation of 1:2 diketones; for instance, diacetyl yields xyloquinone under the influence of alkali (cf. B. **21**, 1411 and p. 370):



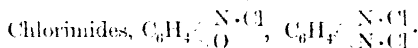
$$\begin{matrix} CH_3\cdot CO\cdot CO\cdot CH\,H_2 \\ +\,H_2\,CH\cdot CO\cdot CO\cdot CH_3 \end{matrix} = \begin{matrix} CH_3\cdot C\cdot CO\cdot CH \\ HC\cdot CO\cdot C\cdot CH_3 \end{matrix} + 2H_2O.$$

o-**Benzoquinone**, $CO\!<\!\begin{matrix} CO\cdot CH \\ CH : CH \end{matrix}\!>\!CH$, isomeric with the *p*-compound, has been recently prepared by *Willstätter* and *Pfannenstiel* (B. 1904, **37**, 4744) by the oxidation of an ethereal solution of catechol (*o*-dihydroxy-benzene) with silver oxide. It forms pale-red transparent plates, is relatively unstable, and begins to decompose at 60°–70°. It is readily reduced by sulphur dioxide to catechol, and dyes the skin brown. For two isomeric forms, cf. B. 1908, **41**, 2580; 1911, **44**, 2632.

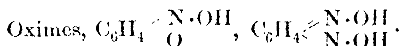
Simple *m*-quinones are not known, but the bimolecular **tribromoresoquinone**, $CO\!<\!\begin{matrix} CBr : CH \\ CBr_2\cdot CO \end{matrix}\!>\!C : C\!<\!\begin{matrix} CH : CBr \\ CO\cdot CBr_2 \end{matrix}\!>\!CO$, has been prepared (B. 1909, **42**, 797, 2814).

F. Quinone Chlorimides, Quinoneaniles, and Anilino-quinones

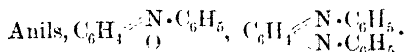
Characteristic N-derivatives of quinones are:



Chlorimides, $C_6H_4\!<\!\begin{matrix} N\cdot Cl \\ O \end{matrix}$, $C_6H_4\!<\!\begin{matrix} N\cdot Cl \\ N\cdot Cl \end{matrix}$.



Oximes, $C_6H_4\!<\!\begin{matrix} N\cdot OH \\ O \end{matrix}$, $C_6H_4\!<\!\begin{matrix} N\cdot OH \\ N\cdot OH \end{matrix}$.



Anils, $C_6H_4\!<\!\begin{matrix} N\cdot C_6H_5 \\ O \end{matrix}$, $C_6H_4\!<\!\begin{matrix} N\cdot C_6H_5 \\ N\cdot C_6H_5 \end{matrix}$.

The **quinone chlorimides** are obtained by the oxidation of the *p*-amino-phenols or *p*-phenylene-diamines with bleaching powder, *e.g.* **quinone chlorimide**, $O:C_6H_4:NCl$, from *p*-amino-phenol hydrochloride, and **quinone dichlorimide**, $Cl\cdot N:C_6H_4:N\cdot Cl$, from *p*-phenylene-diamine hydrochloride. The first-named crystallizes in golden-yellow crystals, which are volatile with steam; when reduced it yields amino-phenol, and when boiled with water quinone; the dichlorimide reacts similarly.

Quinonediimide, $NH:C_6H_4:NH$, forms bright yellow, explosive crystals, and on reduction gives *p*-phenylene-diamine (B. **37**, 1494).

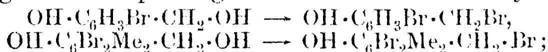
Quinone monoxime, obtained by the action of hydroxylamine hydrochloride on quinone (*H. Goldschmidt*, B. 1884, **17**, 213), is identical with the compound obtained by the action of nitrous acid on phenol, or by the hydrolysis of *p*-nitroso-dimethyl-aniline, and previously termed *p*-nitroso-phenol. It would appear to have the oxime constitution $O:C_6H_4:N\cdot OH$, as with hydroxylamine it yields the dioxime $OH\cdot N:C_6H_4:N\cdot OH$, and when alkylated yields ethers of the type $O:C_6H_4:N\cdot OR$. (Cf. also *Hartley*, J. C. S. 1904, 1016.)

Quinone monanile is obtained by oxidizing *p*-hydroxy-diphenylamine, $OH\cdot C_6H_4\cdot NH\cdot C_6H_5$, and forms fiery-red crystals melting at 97°; with aniline it yields dianilino-quinone anile, $O:C_6H_2(NHPh)_2:NPh$. The dianile is obtained by oxidizing diphenyl-*p*-phenylene-diamine, $C_6H_4(NHPh)_2$; it melts at 175°–180°, and its dianilide, viz. dianilino-quinone dianile, $NPh:C_6H_2(NHPh)_2:NPh$, is most readily obtained by heating *p*-nitroso-dimethyl-aniline with aniline and aniline hydrochloride.

The dyes known as indophenols and indamines are derivatives of quinone-anils. (See Chap. LV, G.)

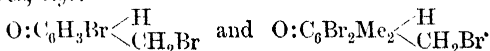
G. Pseudo-phenols. Methylene-quinones

Numerous phenolic alcohols react with halogen hydracids yielding the corresponding esters of the alcohols, *e.g.*:



$$OH\cdot C_6H_3Br\cdot CH_2\cdot OH \longrightarrow OH\cdot C_6H_3Br\cdot CH_2Br,$$
$$OH\cdot C_6Br_2Me_2\cdot CH_2\cdot OH \longrightarrow OH\cdot C_6Br_2Me_2\cdot CH_2\cdot Br;$$

but the products thus obtained are insoluble in alkalis, and are characterized by the reactivity of the bromine atom in the $\cdot CH_2Br$ group. The compounds have been termed by *Auwers* **pseudo-phenols**, and they are usually regarded as *o*- or *p*-quinone derivatives, *e.g.*:



$$O:C_6H_3Br{<}^{H}_{CH_2Br} \quad \text{and} \quad O:C_6Br_2Me_2{<}^{H}_{CH_2Br}.$$

Such compounds readily react with alkalis, losing hydrogen bromide and yielding **methylene-quinones** or **quinomethanes** of the type $O:C_6H_3Br:CH_2$; the majority of these are unstable, and immediately yield condensation products which are insoluble in alkalis (cf. *Auwers*, A. **301**, 203; B. **32**, 2978; **34**, 4256; **36**, 1878; **39**, 435; *Zincke*, A. **320**, 145; **322**, 174; **329**, 1; **353**, 335, 357).

A series of **quinodimethane** compounds has been isolated, *e.g.* $CPh_2:C_6H_4:CPh_2$, **tetraphenylquinodimethane**, yellow crystals, m.-p. 268° (*Tschitschibabin*, B. 1908, **41**, 2770); $C_{10}H_7CPh:C_6H_4:CH_2$, a dark-blue powder (*Schlenk* and *Meyer*, B. 1919, **52 B**, 8).

XXVI. AROMATIC ACIDS

The aromatic acids are analogous to the fatty acids in most respects. As acids they are capable of forming exactly the same kinds of derivatives as the latter, *e.g.* metallic salts, esters, chlorides, anhydrides, amides, &c.:

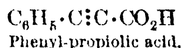
$C_6H_5 \cdot CO_2H$ (benzoic acid).
$C_6H_5 \cdot CO_2C_2H_5$ (ethyl benzoate); $(C_6H_5 \cdot CO)_2O$ (benzoic anhydride);
$C_6H_5 \cdot CO \cdot Cl$ (benzoyl chloride); $C_6H_5 \cdot CO \cdot NH_2$ (benzamide); &c.

As benzene derivatives they yield chloro-, bromo-, iodo-, hydroxy-, nitro-, amino-, and sulphonic acid derivatives, &c., *e.g.*:

$C_6H_4Cl \cdot CO_2H$ (*chloro-benzoic acids*);
$NH_2 \cdot C_6H_4 \cdot CO_2H$ (amino-benzoic acids);
$OH \cdot SO_2 \cdot C_6H_4 \cdot CO_2H$ (sulpho-benzoic acids);
$OH \cdot C_6H_4 \cdot CO_2H$ (hydroxy-benzoic acids);
$C_6H_5 \cdot CH(OH) \cdot CO_2H$ (mandelic acid); &c.

Constitution.—Corresponding with the aromatic acids there are nitriles, *e.g.* with benzoic acid, benzo-nitrile, $C_6H_5 \cdot C{:}N$, which may also be regarded as cyanogen derivatives of the hydrocarbons (in the above case, cyano-benzene), and which, on hydrolysis, yield the acids. From this, and from their general properties, it follows that their constitution must correspond exactly with that of the fatty acids; like the latter they are characterized by the presence of carboxyl, $CO \cdot OH$, in the molecule. There are monobasic, di-, tri-, and up to hexabasic aromatic acids, according to the number of hydrogen atoms in the molecule which are readily replaceable by metallic radicals, *i.e.* according to the number of carboxyl groups.

Numerous unsaturated aromatic acids are known. As unsaturated compounds, they readily form additive compounds with hydrogen, chlorine, hydrogen iodide, and are thereby converted into saturated acids or their substitution products. In most of these additions the benzene nucleus remains unaltered. Their constitution is therefore entirely analogous to that of the acids of the acrylic or propiolic series; they contain a side chain with a double or triple carbon bond:

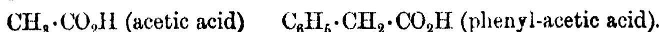
$C_6H_5 \cdot CH:CH \cdot CO_2H$ — Cinnamic acid $C_6H_5 \cdot C⋮C \cdot CO_2H$ — Phenyl-propiolic acid.

In addition to the aromatic acids proper, which have just been mentioned, other acids have been prepared recently, *which are derivatives either of a completely reduced or a partially reduced benzene molecule.* The acids of the former series, *e.g.* the hexahydro-benzoic acids, have properties very similar to those of the saturated fatty acids; while those of the latter, *e.g.* the di- and tetrahydro-benzoic acids, resemble the unsaturated fatty acids. (Cf. p. 377.)

The aromatic hydroxy-acids, *e.g.* the hydroxy-benzoic acids, which are both phenols and acids, manifestly contain phenolic hydroxyl (*i.e.* hydroxyl which is linked directly to the benzene nucleus) in addition to the carboxyl group or groups; they are capable of yielding salts either as acids or as phenols, but otherwise they correspond in many points with the aliphatic hydroxy acids.

The true aromatic hydroxy-acids, such as mandelic acid (phenyl-glycollic acid), which correspond completely with the aliphatic hydroxy-acids, manifestly contain their alcoholic hydroxyl not in the benzene nucleus, but in the side chain, as is also the case with the aromatic alcohols.

Nomenclature.—One of the simplest systems of nomenclature is the designation of the aromatic acids as carboxylic acids of the original hydrocarbons in question, *e.g.* phthalic acid is benzene-1:2-dicarboxylic acid. Many names, such as xylic acid, are taken from those of the hydrocarbons into which the carboxyl has entered, while others, such as mesitylenic acid, indicate the hydrocarbons from which the acids are obtained by oxidation. An important principle as regards nomenclature depends upon the fact that aromatic acids can be derived from almost every fatty acid of any consequence by the exchange of H for C_6H_5, *e.g.*:



$CH_3 \cdot CO_2H$ (acetic acid) $C_6H_5 \cdot CH_2 \cdot CO_2H$ (phenyl-acetic acid).

There thus exist phenylated acids analogous to the acids of the acetic, glycollic, succinic, malic, and tartaric series, &c. For example, atropic acid, $C_6H_5 \cdot C(CO_2H):CH_2$, may be designated α-phenyl-acrylic acid, and cinnamic acid, $C_6H_5 \cdot CH:CH \cdot CO_2H$, β-phenyl-acrylic acid.

Properties.—Most of the aromatic acids are solid crystalline substances, generally only sparingly soluble in water, and therefore precipitated by acids from solutions of their salts, but often readily soluble in alcohol and ether. The simpler among them can be distilled or sublimed without decomposition, while the more complicated, especially phenolic and polycarboxylic acids, evolve carbon dioxide when heated; *e.g.* salicylic acid, $OH \cdot C_6H_4 \cdot CO_2H$, breaks up into phenol and CO_2. The elimination of carbonic anhydride from those acids which volatilize without decomposition may be effected by heating with soda-lime; in polybasic acids the carboxyls may be successively decomposed:



$$C_6H_4(CO_2H)_2 = C_6H_5CO_2H + CO_2 = C_6H_6 + 2CO_2.$$

Occurrence.—A large number of the aromatic acids are found in nature, *e.g.* in many resins and balsams, and also in the animal organism in the form of nitrogeneous derivatives such as hippuric acid (benzoyl-glycocoll), $C_6H_5 \cdot CO \cdot NH \cdot CH_2 \cdot CO_2H$.

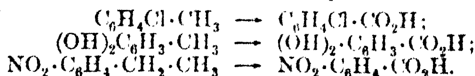
Modes of Formation.—A. Of the saturated acids:—

1. By the oxidation of the corresponding primary alcohols or aldehydes, *e.g.* benzoic acid from benzyl alcohol, or from benzaldehyde.

2. One of the commonest methods of obtaining aromatic acids is by the oxidation of benzene homologues. Each alkyl group present in the nucleus of the hydrocarbon can be oxidized to a carboxylic group, whether it be long or short, *e.g.* both $C_6H_5 \cdot CH_3$ and $C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CH_3$ yield $C_6H_5 \cdot CO_2H$.

All substituted benzene homologues which contain the substituent in the side chain are similarly oxidized to non-substituted aromatic acids, *e.g.* $C_6H_5 \cdot CH_2Cl$, $C_6H_5 \cdot CH_2 \cdot NH_2$, and $C_6H_5 \cdot CH:CH \cdot CO_2H$ yield $C_6H_5 \cdot CO_2H$.

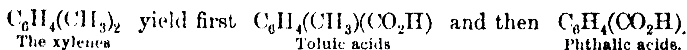
A substituted benzene homologue which contains halogen, nitro-, sulpho-, amino-, hydroxy-, &c., substituents attached to the benzene nucleus, yields a similarly substituted aromatic acid, *e.g.*:



$$C_6H_4Cl \cdot CH_3 \rightarrow C_6H_4Cl \cdot CO_2H;$$
$$(OH)_2C_6H_3 \cdot CH_3 \rightarrow (OH)_2 \cdot C_6H_3 \cdot CO_2H;$$
$$NO_2 \cdot C_6H_4 \cdot CH_2 \cdot CH_3 \rightarrow NO_2 \cdot C_6H_4 \cdot CO_2H.$$

Should there be several side chains in the molecule, they

are usually all converted directly into carboxyl by chromic acid; whereas by using dilute nitric acid, this transformation can be effected step by step, *e.g.*:



$C_6H_4(CH_3)_2$ yield first $C_6H_4(CH_3)(CO_2H)$ and then $C_6H_4(CO_2H)_2$
The xylenes — Toluic acids — Phthalic acids.

Nevertheless, the three classes of isomeric benzene derivatives with two side chains comport themselves differently. The para-compounds are the most readily oxidized to acids by chromic acid mixture, and then the meta-; whereas the ortho compounds are either completely destroyed by it (p. 376), or not attacked at all. The last-named may, however, be oxidized in the normal manner by nitric acid or potassic permanganate. The entrance of a negative group or of hydroxyl into the *o*-position with respect to the alkyl radical renders the oxidation more difficult (cf. p. 145).

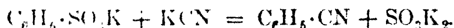
3. By the hydrolysis of the corresponding nitriles:



$$C_6H_5 \cdot CN + 2H_2O = C_6H_5 \cdot CO_2H + NH_3.$$

These nitriles, which can be prepared from the ammonium salts of the acids in the same manner as those of the fatty series, are often obtained by the following syntheses:—

(*a*) By distilling the potassium salts of the sulphonic acids with potassic cyanide or ferrocyanide (*Merz*), just as the nitriles of the fatty acids are formed from the potassium alkyl-sulphates (p. 101):



$$C_6H_5 \cdot SO_3K + KCN = C_6H_5 \cdot CN + SO_3K_2.$$

Nitriles cannot, as a rule, be prepared from KCN and aromatic halogen derivatives which contain the halogen attached to the nucleus (cf. p. 383); the halogen is more readily replaced by cyanogen if sulphonic acid or nitro-groups are likewise present:



$$C_6H_4Br \cdot NO_2 + KCN = CN \cdot C_6H_4 \cdot NO_2 + KBr.$$

Benzyl chloride, $C_6H_5 \cdot CH_2Cl$, and all the haloid hydrocarbons which are substituted in the side chain, on the other hand, react with potassium cyanide in the manner characteristic of the alphyl halides:

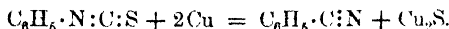


$$C_6H_5 \cdot CH_2Cl + KCN = KCl + C_6H_5 \cdot CH_2 \cdot CN$$
Benzyl cyanide.

(*b*) By diazotizing the primary amines and replacing the diazo-group by cyanogen, according to *Sandmeyer's* reaction

(p. 416). This reaction is frequently made use of in the preparation of substituted benzo-nitriles, *e.g.* 2 : 4-dibromo-benzo-nitrile, $C_6H_3Br_2CN$, and the isomeric 2 : 6-compound, also of tolu-nitriles, $CH_3 \cdot C_6H_4 \cdot CN$.

(*c*) By heating the mustard oils (phenyl-iso-thiocyanates, p. 285), with copper or zinc dust (*Weith*):



$$C_6H_5 \cdot N:C:S + 2Cu = C_6H_5 \cdot C\vdots N + Cu_2S.$$

(*d*) By the molecular transformation of the isomeric iso-nitriles at a somewhat high temperature:



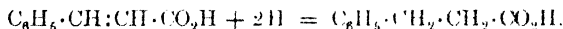
$$C_6H_5 \cdot N:C \longrightarrow C_6H_5 \cdot C\vdots N.$$

(*e*) By eliminating the elements of water from the oximes of the aldehydes by means of acetyl chloride (Chap. XLVI. C.):



$$\text{Benzaldoxime, } C_6H_5 \cdot CH:N \cdot OH = C_6H_5 \cdot CN + H_2O.$$

4. By the reduction of unsaturated acids, thus hydrocinnamic by the reduction of cinnamic acid with sodium amalgam and water, or with hydrogen and finely divided Palladium:



$$C_6H_5 \cdot CH:CH \cdot CO_2H + 2H = C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CO_2H.$$

The acids obtained by this method always contain the CO_2H group attached to a side chain. Similar acids can also be obtained by the reduction of hydroxy-, bromo-, or keto-acids, where the OH, Br, CO, and CO_2H are all in side chains, *e.g.*:



$$C_6H_5 \cdot CH(OH) \cdot CO_2H \longrightarrow C_6H_5 \cdot CH_2 \cdot CO_2H.$$

5. A number of syntheses of nucleus carboxylic acids can be accomplished. These may be regarded as the more or less direct introduction of the carboxylic group into the benzene nucleus, and are usually effected by means of carbonic acid derivatives. In many cases the yields are only small, and the reactions are mainly of theoretical interest.

(*a*) Benzoic acid and its homologues are produced by the action of carbon dioxide upon bromo-benzenes, &c., in presence of sodium (*Kekulé*):



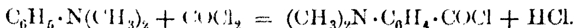
$$C_6H_5Br + CO_2 + 2Na = C_6H_5 \cdot CO_2Na + NaBr.$$

(*b*) By the action of phosgene, $COCl_2$, upon benzene and its homologues in presence of $AlCl_3$ (*Friedel* and *Crafts*):



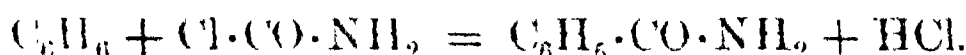
$$C_6H_6 + COCl_2 = C_6H_5 \cdot COCl + HCl.$$

Acid chlorides are first formed, but can be readily decomposed by water. By the further action of these chlorides upon benzene in presence of $AlCl_3$, ketones are formed (see Benzo-phenone). Carbonyl chloride reacts most readily with tertiary amines:



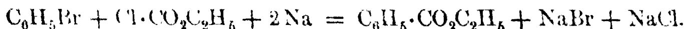
$$C_6H_5 \cdot N(CH_3)_2 + COCl_2 = (CH_3)_2N \cdot C_6H_4 \cdot COCl + HCl.$$

(*c*) By the action of carbamic chloride, $Cl \cdot CO \cdot NH_2$, upon benzene (or phenol) in presence of $AlCl_3$, amides of the aromatic acids are formed, and these can be hydrolysed (*Gatterman*, B. 1899, **32**, 1116):



$$C_6H_6 + Cl \cdot CO \cdot NH_2 = C_6H_5 \cdot CO \cdot NH_2 + HCl.$$

(*d*) By the action of sodium upon a mixture of a brominated benzene and ethyl chloro-carbonate (*Wurtz*); in this case the esters are first formed, but these are readily hydrolysed:



$$C_6H_5Br + Cl \cdot CO_2C_2H_5 + 2\,Na = C_6H_5 \cdot CO_2C_2H_5 + NaBr + NaCl.$$

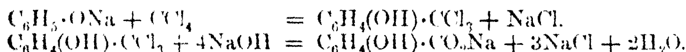
(*e*) The phenolic acids are formed by passing carbon dioxide over heated sodium phenates (*Kolbe*; see Salicylic acid):



$$C_6H_5 \cdot ONa + CO_2 = OH \cdot C_6H_4 \cdot CO_2Na.$$

In the case of the polyhydroxy-phenols, *e.g.* resorcinol, an acid is often formed by merely heating the phenol with a solution of ammonium carbonate or potassium bicarbonate (B. **13**, 930).

(*f*) *p*-Hydroxy-acids are formed by the action of carbon tetrachloride upon phenols in alkaline solution (B. **10**, 2185, *Tiemann-Reimer* reaction; cf. p. 459):



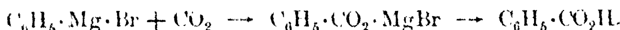
$$C_6H_5 \cdot ONa + CCl_4 = C_6H_4(OH) \cdot CCl_3 + NaCl.$$
$$C_6H_4(OH) \cdot CCl_3 + 4NaOH = C_6H_4(OH) \cdot CO_2Na + 3NaCl + 2H_2O.$$

(*g*) By heating the sulphonates with sodium formate (*V. Meyer*):



$$C_6H_5 \cdot SO_3Na + HCO_2Na = C_6H_5 \cdot CO_2Na + HSO_3Na.$$

(*h*) By the action of carbon dioxide on ethereal solutions of organo-magnesium compounds (*Grignard's* reagents), and subsequent treatment with acids:

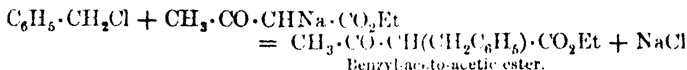


$$C_6H_5 \cdot Mg \cdot Br + CO_2 \longrightarrow C_6H_5 \cdot CO_2 \cdot MgBr \longrightarrow C_6H_5 \cdot CO_2H.$$

6. Syntheses by the aid of ethyl aceto-acetate and ethyl malonate.

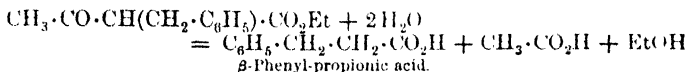
Ethyl aceto-acetate reacts with the halide derivatives which are substituted in the side chain, *e.g.* benzyl chloride, exactly

as in the fatty series, with the formation of the more complicated ketonic acids, which again are capable of undergoing either the "acid hydrolysis" or the "ketonic hydrolysis" (p. 234), *e.g.*:



$$C_6H_5\cdot CH_2Cl + CH_3\cdot CO\cdot CHNa\cdot CO_2Et = CH_3\cdot CO\cdot CH(CH_2C_6H_5)\cdot CO_2Et + NaCl$$

Benzyl-aceto-acetic ester.



$$CH_3\cdot CO\cdot CH(CH_2\cdot C_6H_5)\cdot CO_2Et + 2H_2O = C_6H_5\cdot CH_2\cdot CH_2\cdot CO_2H + CH_3\cdot CO_2H + EtOH$$

β-Phenyl-propionic acid.

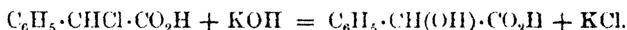
Ethyl phloroglucinol dicarboxylate, $(OH)_3\cdot C_6H(CO_2Et)_2$, may be synthesised by heating ethyl sodio-malonate with ethyl malonate at 145° (*Moore*, J. C. S. 1904, 165).

7. Hydroxy-acids and keto-acids are formed by exactly the same methods as in the fatty series (pp. 213 and 214), *e.g.* mandelic acid by the combination of hydrogen cyanide with benzaldehyde, and hydrolysis of the nitrile thus formed (B. **14**, 239, 1965):



$$C_6H_5\cdot CHO + HCN = C_6H_5\cdot CH(OH)\cdot CN;$$

or from phenyl-chloro-acetic acid (B. **14**, 239):

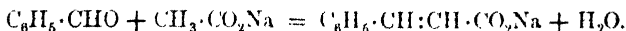


$$C_6H_5\cdot CHCl\cdot CO_2H + KOH = C_6H_5\cdot CH(OH)\cdot CO_2H + KCl.$$

B. The following are some of the commoner methods employed for the preparation of **unsaturated** acids:—

1. From the mono-haloid substitution products of the saturated acids by the elimination of halogen hydracid (cf. p. 169); also from the corresponding nitriles, primary alcohols, &c., as in the case of the saturated compounds.

2. According to the so-called *Perkin* synthesis, by the action of aromatic aldehydes upon the sodium salts of fatty acids in the presence of a condensing agent, usually acetic anhydride. Thus, when benzaldehyde is heated with acetic anhydride and sodium acetate, cinnamic acid is formed:

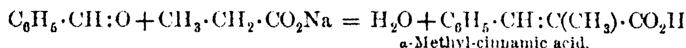


$$C_6H_5\cdot CHO + CH_3\cdot CO_2Na = C_6H_5\cdot CH:CH\cdot CO_2Na + H_2O.$$

The acetic anhydride probably acts as a dehydrating agent in this instance, the reaction taking place between the sodium acetate and the aldehyde (cf. A. **216**, 101). Hydroxy-acids are formed as intermediate products by a reaction similar to the "aldol condensation" (p. 138); in the above case, for instance, β-phenyl-hydracrylic acid, $C_6H_5\cdot CH(OH)\cdot CH_2\cdot CO_2H$.

When the sodium salt and the anhydride of two different acids, *e.g.* sodic propionate and acetic anhydride, are used, the product varies with the conditions (B. 1901, **34**, 918), but usually consists of a mixture of two unsaturated acids.

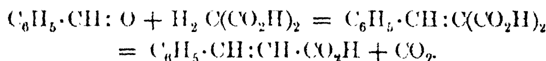
This reaction also takes place with the hydroxy-aldehydes, with the homologues of acetic acid, and also with dibasic acids, *e.g.* malonic; but all acids employed must contain a CH_2 group in the α-position with respect to the CO_2H, *e.g.*:



$$C_6H_5\cdot CH:O + CH_3\cdot CH_2\cdot CO_2Na = H_2O + \underset{\alpha\text{-Methyl-cinnamic acid.}}{C_6H_5\cdot CH:C(CH_3)\cdot CO_2H}$$

It is a very general method used for the preparation of $\alpha:\beta$-unsaturated acids; in certain cases, *e.g.* α-phenyl-cinnamic acid, $C_6H_5\cdot CH:C(C_6H_5)\cdot CO_2H$, and its nitro-derivatives, two stereo-isomerides are produced corresponding with the two crotonic acids or with fumaric and maleic acid.

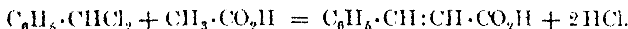
Unsaturated monobasic acids are also formed when aromatic aldehydes are heated with malonic acid in presence of ammonia, aniline, or other amines (*Knoevenagel*):



$$C_6H_5\cdot CH:O + H_2C(CO_2H)_2 = C_6H_5\cdot CH:C(CO_2H)_2$$
$$= C_6H_5\cdot CH:CH\cdot CO_2H + CO_2.$$

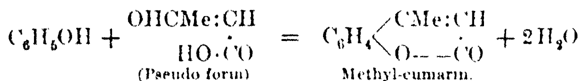
The esters of these acids are formed when aromatic aldehydes are condensed with the esters of fatty acids in the presence of sodium ethoxide (*Claisen*, B. **23**, 976; cf. *Claisen* condensation, p. 232)

3. Cinnamic acid is also formed by the action of benzal chloride upon sodium acetate (*Caro*):



$$C_6H_5\cdot CHCl_2 + CH_3\cdot CO_2H = C_6H_5\cdot CH:CH\cdot CO_2H + 2HCl.$$

4. By the action of aceto-acetic ester upon the phenols in presence of concentrated H_2SO_4, unsaturated phenolic acids or their anhydrides (B. **16**, 2119; **17**, 2191) are formed, *e.g.*:



$$C_6H_5OH + \underset{\text{(Pseudo form)}}{\begin{matrix}OHCMe:CH\\ HO\cdot CO\end{matrix}} = \underset{\text{Methyl-cumarin.}}{C_6H_4\left\langle\begin{matrix}CMe:CH\\ O\text{---}CO\end{matrix}\right.} + 2H_2O$$

A. Monobasic Aromatic Acids

Constitution and Isomers.—The cases of isomerism in the aromatic acids are easy to tabulate. An isomer of benzoic acid is neither theoretically possible nor actually known. Carboxylic acids of the formula $C_8H_8O_2$ may, however, be

Saturated Acids

	Acid	Formula	M.-p.	K.	M.-p. of Amide.
	Benzoic	$C_6H_5 \cdot CO_2H$	121°	0·0060	130°
$C_8H_8O_2$	**Phenyl-acetic**	$C_6H_5 \cdot CH_2 \cdot CO_2H$	76°	0·00556	154°
$C_8H_8O_2$	***o*-Toluic**	$CH_3 \cdot C_6H_4 \cdot CO_2H$	105°	0·0120	139
$C_8H_8O_2$	***m*-Toluic**	Do.	111°	0·00514	
$C_8H_8O_2$	***p*-Toluic**	Do.	180°	0·00515	158°
$C_9H_{10}O_2$	Hydrocinnamic	$C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CO_2H$	49°	0·00227	82°
$C_9H_{10}O_2$	Hydratropic	$CH_3 \cdot CH(C_6H_5) \cdot CO_2H$	liq.	0·00425	91°
$C_9H_{10}O_2$	*o*-Tolyl-acetic	$CH_3 \cdot C_6H_4 \cdot CH_2 \cdot CO_2H$	89°	...	161°
$C_9H_{10}O_2$	*m*-Tolyl-acetic	Do.	61°	...	141°
$C_9H_{10}O_2$	*p*-Tolyl-acetic	Do.	91°	...	184°
$C_9H_{10}O_2$	*o*-Ethyl-benzoic	$C_2H_5 \cdot C_6H_4 \cdot CO_2H$	68°	...	152°
$C_9H_{10}O_2$	*m*-Ethyl-benzoic	Do.	47°	...	...
$C_9H_{10}O_2$	*p*-Ethyl-benzoic	Do.	112°	...	115°
$C_9H_{10}O_2$	Mesitylenic acid	$\underset{3\cdot 5}{(CH_3)_2} \cdot C_6H_3 \cdot \underset{1}{CO_2H}$	166°	...	133°

Hydroxy-saturated Acids

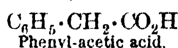
Acid	Formula	M.-p.	K.	M.-p. of Amide.
Salicylic acid (ortho)	$OH \cdot C_6H_4 \cdot CO_2H$	155°	0·102	140°
***m*-Hydroxy-benzoic acid**	Do.	188°	0·0087	170°
***p*-Hydroxy-benzoic acid**	Do.	214°	0·00286	162°
p-Methoxy-benzoic or anisic acid	$CH_3O \cdot C_6H_4 \cdot CO_2H$	184°	0·0032	162°–163°
Mandelic acid	$C_6H_5 \cdot CH(OH) \cdot CO_2H$	118°	0·042	132°
Tropic acid	$C_6H_5 \cdot CH(CH_2 \cdot OH)CO_2H$	117°	0·0075	...

Unsaturated Acids

Acid	Formula	M.-p.	K.	M.-p. of Amide.
Cinnamic acid	$C_6H_5 \cdot CH:CH \cdot CO_2H$	133°	0·00355	147°
Atropic acid	$CH_2:C(C_6H_5) \cdot CO_2H$	106°	0·0143	...
Phenyl-propiolic acid	$C_6H_5C \vdots C \cdot CO_2H$	136°	0·59	100°
Coumaric or *p*-hydroxy-cinnamic acid	$OH \cdot C_6H_4 \cdot CH:CH \cdot CO_2H$	206°	0·00216	..

derived from toluene by the entrance of carboxyl either into the benzene nucleus or into the side chain, thus:





The nature of their oxidation products yields proof of their constitution, the former yielding the phthalic acids, and the latter benzoic.

Of acids $C_9H_{10}O_2$, a large number of isomers are already known (see table). Hydrocinnamic acid and hydratropic acid are phenyl-propionic acids, the former β- and the latter α-, corresponding with the lactic acids; the isomeric relations of the fatty acids thus repeat themselves here. The tolyl-acetic acids, $CH_3 \cdot C_6H_4 \cdot CH_2 \cdot CO_2H$, and the ethyl-benzoic acids, $C_2H_5 \cdot C_6H_4 \cdot CO_2H$, stand in much the same relation to each other as aceto-acetic acid, $CH_3 \cdot CO \cdot CH_2 \cdot CO_2H$, to propionyl-formic acid, $C_2H_5 \cdot CO \cdot CO_2H$, and they all yield phthalic acids when oxidized. Lastly, mesitylenic acid and its isomers are dimethyl benzoic acids, and are oxidizable to benzene-tricarboxylic acids.

As instances of isomers among the unsaturated acids, we may take cinnamic and atropic acids (analogous to β- and α-chlor-acrylic acids, p. 174).

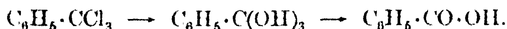
Further, the hydroxy-toluic acids, $C_6H_3(CH_3)(OH)(CO_2H)$, are isomeric with mandelic acid, $C_6H_5 \cdot CH(OH) \cdot CO_2H$, the former being oxidized to hydroxy-phthalic acids, $C_6H_3(OH)(CO_2H)_2$, and the latter to benzoic acid; the hydrocoumaric acids, $C_9H_{10}O_3$, are likewise isomeric with tropic acid. The first-named yield hydroxy-benzoic acids on oxidation, and the last benzoic.

Differences are apparent, *e.g.* in respect to reducibility, according as the carboxyl is linked directly to the nucleus or to a side chain; the amides of the respective acids are in the former case reduced to the corresponding alcohols, but not in the latter. (Cf. B. 24, 173.)

1. MONOBASIC SATURATED ACIDS

Benzoic acid, $C_6H_5 \cdot CO_2H$, was discovered in gum benzoin in 1608, and prepared from urine by *Scheele* in 1785. Its composition was established by *Liebig* and *Wohler's* classical researches in 1832. It occurs in nature in gum benzoin, from which it may be obtained by sublimation ("acidum benzoicum ex resina"); also in dragon's-blood (a resin), in Peru and Tolu balsams, in castoreum, and in cranberries. It

is present in the urine of horses in combination with glycocoll as hippuric acid, from which it may be obtained by hydrolysis with hydrochloric acid ("acidum benzoicum ex urina"). It is obtained on the large scale ("ac. benz. ex toluole") as a by-product in the manufacture of oil of bitter almonds from benzyl chloride or benzal chloride. The acid may also be formed by heating benzo-trichloride with water to a somewhat high temperature:



$$C_6H_5\cdot CCl_3 \rightarrow C_6H_5\cdot C(OH)_3 \rightarrow C_6H_5\cdot CO\cdot OH.$$

Benzoic acid is also present in coal-tar. It crystallizes in colourless glistening plates or flat needles, sublimes readily, and is volatile with steam; its vapour has a peculiar irritating odour, and gives rise to coughing. It melts at 121°, boils at 250°, and is readily soluble in hot water, but only sparingly in cold. When heated with lime, it is decomposed into benzene and carbon dioxide. It is used in medicine and in the manufacture of aniline blue. Some of its salts crystallize beautifully, *e.g.* **calcium benzoate**, $(C_6H_5\cdot CO_2)_2Ca + 3\,H_2O$, in glistening prisms.

From the partially or wholly reduced benzene molecule there are derived (*a*) the **dihydro-benzoic** acids, $C_6H_7\cdot CO_2H$, of which five are theoretically possible, according to the position of the double linkings, viz. Δ-1:3-, Δ-1:4-, Δ-1:5-, Δ-2:4-, and Δ-2:5-dihydro-benzoic acids, but only two known (B. 1891, **24**, 2623, and 1893, **26**, 454); (*b*) the **tetrahydro-benzoic acids**, $C_6H_9\cdot CO_2H$, all three of which are actually known, viz. Δ-1-, Δ-2-, and Δ-3-tetrahydro-benzoic acids (A. **271**, 231); and a **hexahydro-benzoic acid**, $C_6H_{11}\cdot CO_2H$ (*hexamethylene-carboxylic acid*), which is found in the petroleum from Baku, and which can also be prepared from benzoic acid.

The **Esters**, *e.g.* **methyl benzoate**, $C_6H_5\cdot CO_2CH_3$, b.-pt. 199°, and **ethyl benzoate**, $C_6H_5\cdot CO_2C_2H_5$, b.-pt. 213°, are always prepared by the catalytic method of esterification (p. 180), namely, by boiling the acid for three to four hours with a 3-per-cent solution of dry hydrogen chloride or of concentrated sulphuric acid in the requisite alcohol (*E. Fischer* and *Speier*, B. 1895, **28**, 3252). They may also be obtained by the other general methods for the preparation of esters: (*a*) by the action of an acid chloride on the alcohol alone, or in presence of alkali (*Schotten*, *Baumann*) or of pyridine (*Einhorn* and *Hollandt*, Abstr. 1898, **1**, 577); (*b*) by the action of an alkyl iodide on the silver salt of the acid; and (*c*) by the action of alkyl sulphates, more especially methyl sulphate, on aqueous solu-

tions of the alkali salts of the acids (*Werner* and *Seybold*, B. 1904, **37**, 3658). These esters are liquids of pleasant aromatic odour which boil for the most part without decomposition, and frequently serve for the recognition and estimation of alcohols. They may be hydrolysed in much the same manner as the aliphatic esters, although as a rule not so readily.

Benzyl benzoate, $C_6H_5 \cdot CO_2 \cdot CH_2 \cdot C_6H_5$, is present in the balsams of Peru and Tolu.

Benzoyl chloride, $C_6H_5 \cdot CO \cdot Cl$ (*Liebig* and *Wöhler*), obtained by the action of phosphorus pentachloride on the acid, is the complete analogue of acetyl chloride, but more stable than the latter, since it is only slowly hydrolysed by cold water, although quickly by hot. It is a colourless liquid boiling at 198°, and has a most characteristic pungent odour. It is prepared technically by chlorinating benzaldehyde.

Benzoic anhydride, $(C_6H_5 \cdot CO)_2O$ (*Gerhardt*), is exactly analogous to acetic anhydride. It crystallizes in prisms insoluble in water, boils without decomposition, and becomes hydrated on boiling with water. M.-pt. 39°.

In addition to the ordinary anhydrides or oxides, peroxides of the type **benzoyl peroxide** or **benzo-peroxide**, $C_6H_5 \cdot CO \cdot O \cdot O \cdot CO \cdot C_6H_5$, are known They may be obtained by the action of the acid chloride on a cooled solution of sodium peroxide (B. 1900, **33**, 1575, and C. C. 1899, **2**, 396). Benzo-peroxide crystallizes from alcohol in prisms, melts at 106°–108°, is relatively stable, and is insoluble in water. When its ethereal solution is mixed with sodium ethoxide, the products formed are ethyl benzoate, and the sodium salt of **perbenzoic acid**, $C_6H_5 \cdot CO \cdot O \cdot OH$, a hygroscopic acid melting at 41°–43°. It has a strong odour resembling hypochlorous acid, is readily volatile, but decomposes violently when heated, and is a strong oxidizing agent Many aliphatic and aromatic acids yield similar derivatives.

Benzamide, $C_6H_5 \cdot CO \cdot NH_2$, corresponds with acetamide, and is prepared from benzoyl chloride and ammonia or ammonium carbonate. It forms lustrous, nacreous plates, melting at 130°, boils without decomposition, and is readily soluble in hot water.

The amido-hydrogen of benzamide may be substituted by alkyl radicals such as phenyl, &c., with the formation, *e.g.* of **benzanilide**, $C_6H_5 \cdot CO \cdot NHC_6H_5$, the anilide of benzoic acid, a compound which can be readily prepared from aniline and benzoic acid, or aniline and benzoyl chloride. It crystallizes in colourless plates, melts at 158°, distils unchanged, and is

the complete analogue of acetanilide, but is more difficult to hydrolyse, fusion with potash being one of the best methods.

Thio-benzamide, $C_6H_5 \cdot CS \cdot NH_2$, is obtained by the union of benzo-nitrile with hydrogen sulphide, or by heating benzylamine with sulphur.

Benzoyl-hydrazine, *Benzhydrazide*, $C_6H_5 \cdot CO \cdot NH \cdot NH_2$, obtained from ethyl benzoate and hydrazine hydrate, melts at 112°, and with nitrous acid yields **benzoyl-azimide**, *benzazide*, $C_6H_5 \cdot CO \cdot N\langle {N \atop N} \Vert$, which yields benzoic and hydrazoic acids on hydrolysis. (Cf. *Curtius*, Abstr. 1895, **1**, 32.)

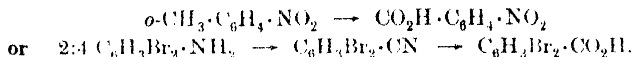
Metallic derivatives of benzamide are also known, *e.g.* **benzamide silver**. *Titherley* (J. C. S. 1897, 468; 1901, 407) has shown that the silver derivative exists in two forms: a white compound, which is stable and is probably $C_6H_5 \cdot C \lesssim {NH \atop OAg}$, and an unstable orange compound, $C_6H_5 \cdot CO \cdot NHAg$. These two metallic derivatives correspond with the pseudo and normal formulæ for benzamide, viz. $C_6H_5 \cdot C \lesssim {NH \atop OH}$ and $C_6H_5 \cdot CO \cdot NH_2$. From the pseudo form are derived imino-ethers (cf. p. 192).

Hippuric acid, *Benzamino-acetic acid*, $C_6H_5 \cdot CO \cdot NH \cdot CH_2 \cdot CO_2H$, is an amino-derivative of benzoic acid, being derived from the latter and glycocoll (amino acetic acid); it may be prepared by heating benzoic anhydride with glycocoll (B. **17**, 1663), and is present in the urine of horses and of other herbivora. When benzoic acid or toluene is taken internally, it is eliminated from the system in the form of hippuric acid. It crystallizes in rhombic prisms, sparingly soluble in cold water but readily in hot, decomposes when heated, and forms salts, esters, nitro-derivatives, &c. When hydrolysed with concentrated hydrochloric acid it yields glycocoll hydrochloride and benzoic acid.

Benzo-nitrile, C_6H_5CN (cf. p. 467), is an oil which smells like oil of bitter almonds, and boils at 191°. It is prepared either by the action of PCl_5 upon benzamide (p. 190), or by distilling benzoic acid with ammonium thiocyanate. It possesses all the properties of a nitrile, combining slowly with nascent hydrogen to benzylamine, readily with halogen hydride to an imino-chloride, with amines to amidines (p. 194; cf. A. **192**, 1), with hydroxylamine to amidoximes (p. 195). With hydrogen peroxide it yields benzamide.

Substituted Benzoic Acids.—The hydrogen atoms of benzoic acid are replaceable by halogen with the formation *e.g.* of chloro-benzoic acid, $C_6H_4Cl \cdot CO_2H$. In such formation of mono-substitution products the halogen takes up the meta-position with respect to the carboxyl. Nitric acid (especially a mixture of nitric and sulphuric acids) nitrates it readily, *m*-nitro-benzoic acid being the chief product, together with a smaller quantity of the ortho- and a very little of the para-acid.

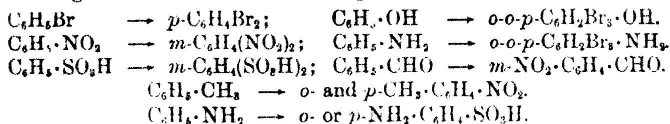
The *o*- and *p*-halogen and nitro-compounds are usually prepared by indirect methods, *e.g.*:



$$o\text{-}CH_3 \cdot C_6H_4 \cdot NO_2 \rightarrow CO_2H \cdot C_6H_4 \cdot NO_2$$

or $$2{:}4\ C_6H_3Br_2 \cdot NH_2 \rightarrow C_6H_3Br_2 \cdot CN \rightarrow C_6H_3Br_2 \cdot CO_2H.$$

In the preceding pages attention has been drawn repeatedly to the influence which a radical, already present in the benzene molecule, exerts on the position taken up by a second radical entering the molecule. As examples we have:



$$C_6H_5Br \rightarrow p\text{-}C_6H_4Br_2; \quad C_6H_5 \cdot OH \rightarrow o\text{-}o\text{-}p\text{-}C_6H_2Br_3 \cdot OH.$$
$$C_6H_5 \cdot NO_2 \rightarrow m\text{-}C_6H_4(NO_2)_2; \quad C_6H_5 \cdot NH_2 \rightarrow o\text{-}o\text{-}p\text{-}C_6H_2Br_3 \cdot NH_2.$$
$$C_6H_5 \cdot SO_3H \rightarrow m\text{-}C_6H_4(SO_3H)_2; \quad C_6H_5 \cdot CHO \rightarrow m\text{-}NO_2 \cdot C_6H_4 \cdot CHO.$$
$$C_6H_5 \cdot CH_3 \rightarrow o\text{- and } p\text{-}CH_3 \cdot C_6H_4 \cdot NO_2.$$
$$C_6H_5 \cdot NH_2 \rightarrow o\text{- or } p\text{-}NH_2 \cdot C_6H_4 \cdot SO_3H.$$

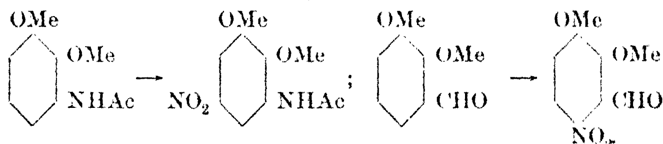
The following rules will be found to apply to most cases:—

I. If the radical already present is Cl, Br, I, OH, NH_2, or CH_3, then, by the introduction of Cl, Br, I, NO_2, or SO_3H radicals, para- and to a certain extent ortho-compounds are formed, and only very exceptionally meta-compounds.

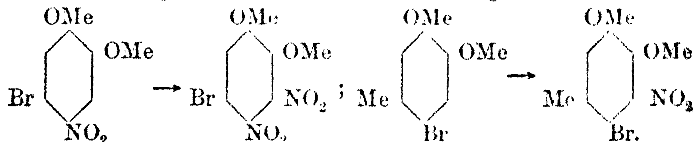
II. If the radical present is NO_2, SO_3H, CHO, or CO_2H, then, on chlorination, bromination, nitration, or sulphonation, meta-compounds are formed. (See *Crum Brown* and *Gibson*, J. C. S. 1892, 367. For details cf. *Obermüller*, Die Orientierende Einflüsse in der Benzolkern, 1909; *Hollemann*, Die Direkte Einführung von Substituenten, 1910; also *Prins*, Abs. 1919, i, 71.)

In many reactions all three isomeric products have been isolated, but in very different quantities; thus at 0° benzoic acid yields 80·2 per cent of *m*, 18·5 of *o*, and only 1·3 of *p*-nitro-benzoic acid; at 30° nitrobenzene yields 91 per cent of *m*-, 8 of *o*-, and 1 of *p*-dinitro-benzene. It is probable that the three isomerides are also formed in other cases which have not been examined so carefully. The temperature at which the substitution occurs also appears to determine to a certain extent the relative proportions of the isomers formed.

When two or more substituents are already present, it is difficult to predict the position which a new group, *e.g.* NO_2, Br, will assume. The groups present may have opposing effects on the entrant or they may have a cumulative effect. As a rule, in the chlorination of a mixed benzene derivative the NH_2 group has the greatest directing influence, and then follow OH, OMe, and NHAc (B.A. Rep. 1915, 83; *Fuchs*, M. 1917, **38**, 331). Occasionally unexpected results are obtained, thus the acetyl group when introduced into *sym. m*-xylenol methyl ether (4:5-dimethylanisole) takes the *o*- and not the *p*-position relative to the OMe group. (*Auwers*, B. 1915, **48**, 90.) Substitution in the veratrole (1:2-dimethoxybenzene) series has been studied in detail (*Jones* and *Robinson*, J. C. S. 1917, **111**, 903). When veratrole is brominated or nitrated, it yields the 4-substituted derivative, and when further nitrated or brominated, the 4:5-substitution products, *i.e.* the Br and NO_2, enter the positions para to the OMe groups. An exception is, however, met with in the case of 4-nitroveratrole, which on bromination yields 6-bromo- 4-nitroveratrole. When an ortho-substituent is already present in the veratrole molecule, the position taken up by the entrant is generally influenced by the polarity of the first substituent, in the sense that when this is positive it enhances, and when negative counteracts the influence of the neighbouring OMe groups, *e.g.*:



With a 4:5-disubstituted derivative a further NO_2 group takes up the position ortho to the more negative substituent.



Vörlander (B. 1919, **52 B**, 263) gives the following classification. 1. Meta-orientating: SO_3H, NO_2, CHO, CO_2H, CO_2R, $CONH_2$, COR, $CO{\cdot}CO_2H$, CN, CCl_3, NH_3X, NR_3X. 2. Ortho- and para-orientating: OH, OR, OAc, NH_2, NHR, NR_2, NHAc, N:N, CH_3 &c., CH_2Cl, $CH_2{\cdot}O{\cdot}NO_2$, $CH_2{\cdot}SO_3H$,

$CH_2\cdot NH_2$, $CH_2\cdot CN$, $CH_2\cdot CO_2H$, $CH_2\cdot CH_2\cdot CO_2H$, $CH:CH\cdot CO_2H$, $CH:CHNO_2$, $C:C\cdot CO_2H$, C_6H_5.

The orientating influence of a positive pole* directly attached to the nucleus is exclusively *m*-directing. A negative pole has a strong *o-p*-directing influence, *e.g.* phenols and thiophenols in alkaline solution. Dipoles such as nitro- and sulphone-groups act the same as if they were free poles with a charge corresponding with that of the dipole nearer the nucleus. Thus both NO_2 and SO_2 have an *m*-orientating effect due to the + charge on the N and S atoms. In all three cases the given directing effect is diminished by the interposition of CH_2 groups between the substituent and the nucleus, cf. phenyltrimethylammonium, benzyltrimethyl-, β-phenylethyltrimethyl- and γ-phenylpropyltrimethyl ammonium salts (*Ingold* and others, J. C. S. 1926, 1562, 1655, 2440). The interposition of $\cdot CH:CH\cdot$ produces a more powerful diminution than does $\cdot CH_2\cdot CH_2\cdot$ Also *m*-orientation decreases regularly with the atomic number of the charged atom. Generally the stronger the *m*-orientation the slower is the rate of substitution. For general discussion of experimental observations and theoretical deductions see *Ingold*, Rep. 1926, 129; 1927, 148; 1928, 137, and J. C. S. 1929, 2257.

SUBSTITUTED BENZOIC ACIDS

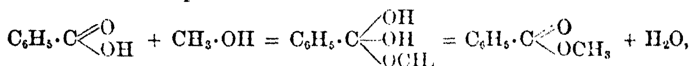
Acid	M.-p.	K.	Ethyl ester. M.-p.	Ethyl ester. B.-p.
Benzoic	121°	0·006	..	211°
o-Methyl-benzoic	105°	0·012	..	220°
m-Methyl-benzoic	110°	0 00514	..	225°
p-Methyl-benzoic	180°	0 00515	..	228°
o Bromo-benzoic	150	0 145	..	254°
m-Bromo-benzoic	155	0 0137	..	259°
p-Bromo-benzoic	251°	..	..	262°
o-Nitro-benzoic	148°	0 616	30°	..
m-Nitro benzoic	141°	0·0345	47°	298°
p-Nitro-benzoic	240°	0 0396	57°	..
o-Amino-benzoic	145°	0 001	13°	267°
m-Amino benzoic	176°	0·003	..	291°
p-Amino-benzoic	186°	0 001	89°	..

The numbers for K given in the table indicate that the introduction of negative radicals, *e.g.* NO_2, Br, &c., more especially into the ortho-position, markedly increases the strength of the acid, whereas the introduction of positive radicals, *e.g.* the amino-, more especially into ortho-positions, tends to weaken the acid (cf. p. 174).

Chemical Retardation and Influence of Substituents (cf. p. 181).—Within recent years a number of examples of the retardation of complete inhibition of chemical reactions by the

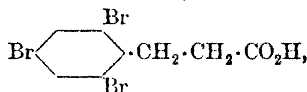
* The seat of a charge in a complex ion is termed a *pole*.

presence of ortho-substituents have been discovered. One of the best known examples of this is met with in the esterification of aromatic acids by the hydrogen chloride catalytic method. *Kellas* (Zeit. Phys. Chem., 1897, **24**, 221) has shown that even one ortho-substituent, whether it be CH_3, NO_2, Br, &c., retards the formation of ester; and *V. Meyer* and *Sudborough* (B. 1894, **27**, 510, 1580, and 3146) have shown that when two such ortho-substituents are present an ester is not formed at all.* The general view is that in the formation of an ester an additive compound of the acid and alcohol,



$$C_6H_5\cdot C\begin{matrix}\nearrow O\\ \searrow OH\end{matrix} + CH_3\cdot OH = C_6H_5\cdot C\begin{matrix}\nearrow OH\\ -OH\\ \searrow OCH_3\end{matrix} = C_6H_5\cdot C\begin{matrix}\nearrow O\\ \searrow OCH_3\end{matrix} + H_2O,$$

is first formed, that this compound then decomposes into the ester and water, and that the spatial arrangements are such that ortho-substituents are so close to the carboxylic group that they interfere with the formation of an additive compound, and thus retard or inhibit esterification (*Wegscheider*). In confirmation of this view we have the fact that *o*-substituents do not interfere to nearly the same extent when the carboxylic group is removed some distance, *e.g.* by the interposition of a chain of carbon atoms. The acid,



s-tribromo-hydrocinnamic acid, for example, is readily esterified under the usual conditions. Other cases of chemical retardation due to *o*-substituents have been met with in the hydrolysis of substituted benzo-nitriles. Di-ortho-substituted benzoyl chlorides and benzamides and benzoic esters are also remarkably stable and difficult to hydrolyse to the acids (*Sudborough, Ira Remsen*). Di-ortho-substituted ketones, *e.g.* 2:6-dimethylacetophenone, cannot be converted into oximes (*V. Meyer*), and di-ortho-substituted tertiary amines, 2:6-dibromo-dimethylaniline, cannot yield quaternary ammonium salts (p. 407) (*E. Fischer*), and di-ortho-substituted anilines do not yield alkylthiocarbimides with thiocarbonyl chloride (J. C. S. 1926, 3041).

That ortho-substituents do not retard or inhibit all chemical actions is shown by the fact that esters of di-ortho-substituted benzoic acids may be obtained by other methods, viz. the

* Esters of such acids can be prepared by heating the acids with alcohol to high temperatures.

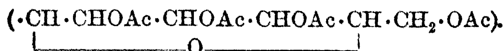
action of the alcohol on the acid chloride, and the action of alkyl iodide on the silver salt of the acid, or of methyl sulphate on an alkali salt of the acid.

In certain reactions the presence of ortho-substituents appears to favour or accelerate a chemical reaction; examples of this are to be met with in the diacetylation of arylamines (*Sudborough*, J. C. S. 1901, **79**, 533) and in the chemical reactivity of picryl chloride, 2:4:6-trinitrochlorobenzene, and similar compounds; see also pages 390, 402, 443.

For discussion of the reactivity of nuclear groups in *o*- and *p*-positions with respect to hydroxy and amino groups or of other groups in *o*- and *p*-positions with respect to nitro carboxylic and sulphonic groups see J. I. I. S. 1915, **2**, 133; Rec. 1926, **45**, 19 and Rep. 1929, 132 for electronic theory. Such reactions are frequently of value for deciding questions of orientation particularly in the diphenyl series (*Turner*, J. C. S. 1927, 1168; 1928, 1168; 1929, 512), thus the ready displacement of halogen by the piperidyl group in a chloro-nitro-diphenyl compound is a proof that the halogen is in the ortho or para position with respect to one of the nitro groups.

The **amino-benzoic acids**, $NH_2 \cdot C_6H_4 \cdot CO_2H$, which are obtained by the reduction of the nitro-acids with tin and hydrochloric acid, &c., are interesting, as they are both bases and acids, *i.e.* **amphoteric**, and therefore similar to glycocoll in chemical character; they combine with hydrochloric acid, chloro-platinic acid, &c., as well as reacting with mineral bases to yield metallic salts. With regard to their constitution, cf. Glycocoll, p. 220. With nitrous acid they yield **diazo-benzoic acids**, $C_6H_4<\genfrac{}{}{0pt}{}{N:N}{CO_2}>$, which correspond with the diazo-benzene-sulphonic acids (p. 435).

The salts derived from amino- and hydroxybenzoic acids are frequently represented by formulæ of the type, $C_6H_4<\genfrac{}{}{0pt}{}{NH_2}{COOM}$, in which the metal is attached to O or N by subsidiary valencies. Such a formula accounts to a certain extent for the fact that silver salicylate and tetraacetobromoglucose (Chap. XLII, B.) yield both $OH \cdot C_6H_4 \cdot COOX$ and $OX \cdot C_6H_4 \cdot COOH$, where X = the tetracetylglucose residue



o-**Amino-benzoic acid** is also obtained from phthalimide, $C_6H_4<{CO \atop CO}>NH$, by the *Hofmann* reaction (cf. Amides, behaviour of, par. 5), and by the oxidation of indigo with manganese dioxide and caustic soda, and is often termed **anthranilic acid**; it forms (in contradistinction to the *m*- and *p*-acids) an intramolecular anhydride, **anthranil**, $C_6H_4<{CO \atop NH}>$, and is an important intermediate product in the synthesis of indigo. The methyl ester is an important constituent of the essential oil of orange-blossom.

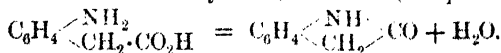
The **sulpho-benzoic acids**, $OH{\cdot}SO_2{\cdot}C_6H_4{\cdot}CO{\cdot}OH$, are dibasic acids. An ammonia derivative of *o*-sulpho-benzoic acid is the sweet substance "**saccharine**", $C_6H_4<{SO_2 \atop CO}>NH$, *i.e.* *o*-sulpho-benzimide, or *o*-benzoyl-sulphone-imide, an imide comparable with succinimide. It is a white crystalline powder, almost three hundred times as sweet as cane-sugar, and is used to some extent in place of the latter.

Acids, $C_8H_8O_2$.—1. The three **toluic acids**, $CH_3{\cdot}C_6H_4{\cdot}CO_2H$, can be prepared from the three xylenes. *p*-**Toluic acid** is obtained from *p*-toluidine, by transforming it—according to the *Sandmeyer* reaction—into *p*-cyano-toluene and hydrolysing the latter (A. **258**, 9). Isomeric with them is—

2. **Phenyl-acetic acid**, *a-Toluic acid*, $C_6H_5 \cdot CH_2 \cdot CO_2H$ (*Cannizzaro*, 1855).—This acid differs characteristically from its isomers by its behaviour upon oxidation (see p. 473). It may be obtained synthetically from benzyl chloride and potassium cyanide, **benzyl cyanide**, $C_6H_5{\cdot}CH_2{\cdot}CN$ (b.-pt. 232°), being formed as intermediate product; it crystallizes in lustrous plates, melts at 76°, and boils at 262°.

It is capable of undergoing substitution either in the benzene nucleus or in the side chain.

Phenyl-chloracetic acid, $C_6H_5{\cdot}CHCl{\cdot}CO_2H$, and **phenyl-aminc-acetic acid**, $C_6H_5{\cdot}CH(NH_2){\cdot}CO_2H$, compounds which possess precisely the same character as mono-chloracetic and amino-acetic acids. Isomeric with phenyl-amino-acetic acid are the three **amino-phenyl-acetic acids**, $NH_2{\cdot}C_6H_4{\cdot}CH_2{\cdot}CO_2H$, of which the *o*-acid is interesting on account of its close relation to the indigo-group. It does not exist in the free state, but forms an intramolecular anhydride, oxindole (Chap. XXXV):



$$C_6H_4<{NH_2 \atop CH_2{\cdot}CO_2H} = C_6H_4<{NH \atop CH_2}>CO + H_2O.$$

The formation of an intramolecular anhydride is of very frequent occurrence in ortho-amino-compounds of this kind, in contradistinction to the *m*- and *p*-compounds (see Indole). Theoretically, it may take place in the above instance in two different ways, viz. either by the elimination of a hydrogen atom of the amino-group together with OH of the carboxyl, or of both of the amino-hydrogen atoms with the oxygen atom from the carbonyl-group. These two cases are distinguished by *Baeyer* as "**Lactam formation**" and "**Lactim formation**". Oxindole is the lactam of *o*-amino-phenylacetic acid, isatin, $C_6H_4<{NH \atop CO}>CO$ (p. 557), the lactam of *o*-amino-phenylglyoxylic acid, $NH_2 \cdot C_6H_4 \cdot CO \cdot CO \cdot OH$, and carbostyril (p. 486), $C_6H_4<{N=C \cdot OH \atop CH:CH}$, the lactim of *o*-amino-cinnamic acid.

Both lactams and lactims contain hydrogen which is readily replaceable; in the former case it is present in the amino-group, and in the latter in the hydroxyl.

If the compounds which result from the replacement of hydrogen by alkyl are very stable, the alkyl in them is linked to the nitrogen, and they are derivatives of the lactams; if, on the contrary, they are easily saponifiable, the alkyl is linked to oxygen, and they are ethers of the lactims. Many lactams and lactims react as tautomeric substances (cf. Isatin and chapter on Constitution and Physical Properties).

Acids, $C_9H_{10}O_2$.—1. Dimethyl-benzoic acids, *Xylene-carboxylic acids*, $C_6H_3Me_2 \cdot CO_2H$. Of these six are possible, and four are known. **Mesitylenic acid,** ($CO_2H:CH_3:CH_3$ = 1:3:5), is prepared by the oxidation of mesitylene. Isomeric with them are—2. The **Phenyl-propionic acids.**

β-Phenyl-propionic acid or **hydrocinnamic acid,** $C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CO_2H$, is prepared by reducing cinnamic acid with sodium amalgam, or with hydrogen in presence of colloidal palladium, and is also formed during the decay of albuminous matter. It crystallizes in slender needles; m.-pt. 48°, b.-pt. 280°.

Many substitution products of this acid are known, among which may be mentioned *o*-**nitro-cinnamic acid dibromide,** $NO_2 \cdot C_6H_4 \cdot CHBr \cdot CHBr \cdot CO_2H$, a compound nearly related to indigo (p. 559); further, **β-phenyl-α amino-propionic acid** (phenyl-alanine), $C_6H_5 \cdot CH_2 \cdot CH(NH_2) \cdot CO_2H$, and **β-phenyl-β-amino-propionic acid,** $C_6H_5 \cdot CH(NH_2) \cdot CH_2 \cdot CO_2H$, both of which can be prepared synthetically, the former being like-

wise produced during the decay of albumen and during the germination of *Lupinus luteus.*

o-**Amino-hydrocinnamic acid**, $NH_2 \cdot C_6H_4 \cdot CH_2 \cdot CH_2 \cdot CO_2H$, is not stable, but is immediately transformed into its lactim, **hydrocarbostyril** (cf. quinoline, Chap. XXXVIII, A. 2).

Hydratropic acid, *a-Phenyl-propionic acid*, $CH_3 \cdot CH(C_6H_5) \cdot CO_2H$, is obtained—as its name implies—by the addition of hydrogen to atropic acid. It is liquid and volatile with steam.

2. MONOBASIC UNSATURATED ACIDS

1. **Cinnamic acid**, $C_6H_5 \cdot CH:CH \cdot CO_2H$ (*Trommsdorf*, 1780), occurs in Peru and Tolu balsams and also in storax, and may be prepared as given at p. 468. It crystallizes in needles or prisms, dissolves readily in hot water, melts at 133°, and boils at 300°. When fused with potash, it is split up into benzoic and acetic acids; it also yields benzoic acid when oxidized. It yields salts, esters, &c.; also additive compounds, with chlorine, bromine, hydrogen chloride, bromide, iodide, and also with hydrogen and hypochlorous acid, *e.g.* cinnamic acid dibromide (β-phenyl-*a*-β-dibromo-propionic acid), $C_6H_5 \cdot CHBr \cdot CHBr \cdot CO_2H$. Further, the hydrogen in the benzene nucleus may be replaced by Cl, Br, NO_2, NH_2, &c.

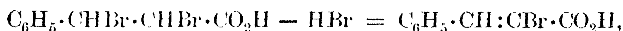
Cinnamic Acids.—According to the ordinary stereo-chemical theory of unsaturated compounds, two cinnamic acids of the formula $C_6H_5 \cdot CH:CH \cdot CO_2H$ should exist (cf. Maleic and Fumaric acids, p. 251). Two have been known for some time, viz. storax-cinnamic acid, melting at 134°, and *allo*-cinnamic acid, melting at 68°, and prepared by reducing β-brom-allo-cinnamic acid with zinc and alcohol, or by reducing phenyl-propiolic acid with hydrogen and finely divided palladium. But, in addition to these, several other cinnamic acids have been described (for summary see *Erlenmeyer*, Biochem. Zeitsch. 1911, **34**, 306): (*a*) *Liebermann's* iso-cinnamic acid (B. 1890, **23**, 141, 512), melting at 58°–59°; this occurs naturally together with the allo acid in cocaine alkaloids, and may also be obtained by fractionally crystallizing the brucine salt of allo-cinnamic acid (B. 1905, **38**, 2562), and decomposing with acid, or by the action of an alcoholic solution of zinc bromide on allo-cinnamic acid (B 1905, **38**, 837). (*b*) *Erlenmeyer's* iso-cinnamic acid, melting at 37°–38°, and obtained by reducing *a*-brom-allo-cinnamic acid with zinc and alcohol (A. 1895, **287**, 1; B. 1904, **37**, 3361). (*c*) Triclinic cinnamic acid,

melting at 80°. (*d*) Hetero-cinnamic acid, m.-pt. 131°. It is probable that the *allo*- and two *iso*-acids are trimorphous forms of the same substance (*Biilmann*, B. **42**, 182, 1443, **43**, 568). They appear to give the same melt as shown by examination of refractive indices (*Stobbe*), and solubilities (*Meyer*), and also to give the same solutions as shown by their electrical conductivities (*Bjerum*, B. **43**, 571), and absorption spectra (*Stobbe*, *ibid.*, 504). Any one of the three acids can be obtained from the melt by impregnating under suitable conditions with a crystal of the desired form; and even the solids are mutually transformable (*Stobbe*, B. **44**, 2735; *Meyer*, 2966; *Stobbe* and *Schönberg*, A., 1913, **402**, 187).

Other authorities deny the existence of the hetero acid (B. **43**, 453, and Abs. 1919, i, 486).

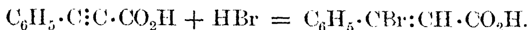
According to *Stoermer* and *Heymann* ordinary cinnamic acid has the trans and the allo acid the cis configuration. This conclusion is based on the fact that the *o*-amino-allo-cinnamic acid which yields coumarin (p. 494) when diazotized and boiled with water, and hence the acid in which the benzene nucleus and the CO_2H group are in cis positions, is the acid which yields allo-cinnamic acid when the amino-group is removed. And the isomeric amino-acid which yields *o*-coumaric acid is the one which gives ordinary cinnamic acid (B. 1912, **45**, 3099).

Although some six cinnamic acids are known, only two α-bromo-cinnamic acids and two β-bromo-cinnamic acids have been prepared. The α-bromo- and α-brom-allo-cinnamic acids are obtained by the elimination of hydrogen bromide from cinnamic acid dibromide:



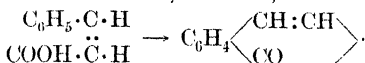
$$C_6H_5{\cdot}CHBr{\cdot}CHBr{\cdot}CO_2H - HBr = C_6H_5{\cdot}CH{:}CBr{\cdot}CO_2H,$$

or its esters, and they melt respectively at 131° and 120°. The corresponding β-acids can be prepared by the addition of hydrogen bromide to phenyl-propiolic acid:



$$C_6H_5{\cdot}C{\vdots}C{\cdot}CO_2H + HBr = C_6H_5{\cdot}CBr{:}CH{\cdot}CO_2H.$$

They melt respectively at 135° and 159°. (Compare *Sudborough* and others, J. C. S. 1903, 666, 1153; 1905, 1841; 1906, 105; 1911, 1620.) The two isomerides in each case represent the cis and trans forms. The cis forms are characterized by the readiness with which they yield cyclic indenones in the presence of sulphuric acid, *Liebermann*, B. 1898, 2096:



$$\begin{matrix} C_6H_5{\cdot}C{\cdot}H \\ COOH{\cdot}\ddot{C}{\cdot}H \end{matrix} \rightarrow C_6H_4\left\langle\begin{matrix} CH{:}CH \\ CO \end{matrix}\right\rangle.$$

o- and *p*-**Nitro-cinnamic acids**, $NO_2 \cdot C_6H_4 \cdot CH{:}CH \cdot CO_2H$, the first of which is of importance on account of its relation to indigo, are obtained by the nitration of cinnamic acid. On reduction the former yields *o*-**amino-cinnamic acid**, which readily yields its lactim **carbostyril** (α-hydroxy-quinoline).

2. **Atropic acid**, $CH_2{:}C(C_6H_5) \cdot CO_2H$, is a decomposition product of atropine. It crystallizes in monoclinic plates, and can be distilled with steam. It breaks up into formic and α-toluic acids when fused with potash.

3. (γ)-**Phenyl-isocrotonic acid**, $C_6H_5 \cdot CH{:}CH \cdot CH_2 \cdot CO_2H$, is formed when benzaldehyde is heated with sodium succinate and acetic anhydride (*W. H. Perkin, sen.*, also *Jayne*, A. **216**, 100):

$$C_6H_5 \cdot CHO + CH_2(CO_2H) \cdot CH_2 \cdot CO_2H - H_2O$$
$$= \begin{array}{l} C_6H_5 \cdot CH \cdot CH(CO_2H) \cdot CH_2 \\ \quad\quad O \text{———————} CO \end{array}$$
$$= CO_2 + C_6H_5 \cdot CH{:}CH \cdot CH_2 \cdot CO_2H.$$

It is of interest on account of its conversion into α-naphthol (see this), $C_{10}H_7 \cdot OH$, upon boiling.

4. **Phenyl-propiolic acid**, $C_6H_5 \cdot C{:}C \cdot CO_2H$ (*Glaser*, 1870), is prepared from cinnamic acid dibromide or its ethyl ester by first converting into α-brom-cinnamic acid by elimination of hydrogen bromide, and then into the acetylenic acid by further elimination (just as ethylene is converted by bromine into ethylene bromide, and the latter decomposed into acetylene by potash). It crystallizes in long needles, and melts at 136°–137°. When heated with water to 120°, it breaks up into CO_2 and phenyl-acetylene (p. 381). It can be reduced to hydrocinnamic acid and transformed into benzoyl-acetic acid.

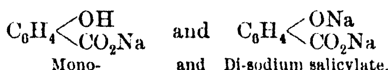
o-**Nitro-phenyl-propiolic acid**, $NO_2 \cdot C_6H_4 \cdot C{:}C \cdot CO_2H$ (*Baeyer*), is prepared in a manner analogous to that just given, viz. by the addition of bromine to ethyl *o*-nitro-cinnamate and treatment of the resulting bromide with alcoholic potash (A. **212**, 240). It is of interest on account of its relation to indigo (see p. 559). It breaks up into CO_2 and *o*-nitro-phenyl-acetylene when heated.

3. SATURATED PHENOLIC ACIDS

(For *modes of formation*, see p. 469.) These acids may also be obtained by the oxidation of the homologues of phenol

and of the hydroxy-aldehydes, which is effected, among other methods, by fusion with alkalis.

The phenolic acids form salts both as carboxylic acids and as phenols, salicylic acid, for instance, the two following classes:



$$C_6H_4<^{OH}_{CO_2Na} \quad \text{and} \quad C_6H_4<^{ONa}_{CO_2Na}$$

Mono- and Di-sodium salicylate.

The first of these two salts is not decomposed by CO_2, while the second, as the salt of a phenol, is decomposed by it and converted into the first. The phenolic acids behave, therefore, like monobasic acids towards sodium carbonate. When both of the hydrogen atoms are replaced by alkyl, there are formed compounds such as $C_2H_5O \cdot C_6H_4 \cdot CO_2C_2H_5$, which, as both ethers and esters, are only half hydrolysed when boiled with potash, *e.g.* to $C_2H_5O \cdot C_6H_4 \cdot CO_2H$, ethyl salicylic acid. The ether acids thus formed possess completely the character of monobasic acids, their alphyl radical being only eliminated by hydriodic acid at a rather high temperature. (Cf. p. 441.)

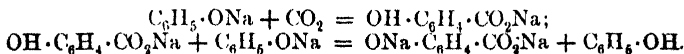
The *o*-hydroxy-acids ($CO_2H:OH = 1:2$) are, in contradistinction to their isomers, volatile with steam, give a violet or blue coloration with ferric chloride, and are readily soluble in cold chloroform.

The *m*-hydroxy-acids are more stable than the *o*- and *p*-compounds; while most of the latter break up into carbon dioxide and phenols when quickly heated, or when acted on by hydro chloric acid at 220°, the former remain unaltered.

The phenolic acids are much more easily converted into halogen or nitro-substitution products than the monobasic acids, just as the phenols are far more readily attacked than the benzene hydrocarbons.

Salicylic acid, *o-Hydroxy-benzoic acid* ($CO_2H:OH = 1:2$) was discovered by *Piria* in 1839. It occurs in the blossom of *Spiræa Ulmaria*, and as its methyl ester in oil of winter-green, &c. It may be obtained by the oxidation of the glucoside saligenin; by fusing coumarin, indigo, *o*-cresol, &c., with potash; by diazotizing *o*-amino-benzoic acid, &c. (see p. 415).

Preparation.—Sodium phenoxide is heated in a stream of carbon dioxide at 180°–220° (*Kolbe*, A. **113**, 125; **115**, 201, &c.), when half of the phenol distils over and basic salicylate of sodium remains behind:



$$C_6H_5 \cdot ONa + CO_2 = OH \cdot C_6H_4 \cdot CO_2Na;$$
$$OH \cdot C_6H_4 \cdot CO_2Na + C_6H_5 \cdot ONa = ONa \cdot C_6H_4 \cdot CO_2Na + C_6H_5 \cdot OH.$$

When C_6H_5OK is used, the product is salicylic acid, provided the temperature is kept below 150°; at higher temperatures, *e.g.* 220°, the para acid is formed. Mono-potassium salicylate, $C_6H_4(OH)\cdot CO_2K$, decomposes in an analogous manner at 220° into phenol and di-potassium *p*-hydroxy-benzoate.

As *Kolbe's* original method of preparation converted only 50 per cent of the phenol into salicylic acid, *Schmitt* devised the following modification:—The sodium phenoxide is heated in a closed vessel with carbon dioxide at 130°, and the compound first formed, $C_6H_5\cdot O\cdot C\begin{smallmatrix}\diagup ONa\\ \diagdown O\end{smallmatrix}$, sodium phenyl-carbonate, is thus transformed into mono-sodium salicylate by the exchange of the $\cdot CO\cdot ONa$ group with the ortho-hydrogen atom of the phenyl radical. (Cf. B. 1905, **38**, 1375; A. 1907, **351**, 313; C.C. 1907, ii, 48.)

Salicylic acid crystallizes in colourless four-sided monoclinic prisms, dissolves sparingly in cold water but readily in hot: it melts at 155°, can be sublimed, but is decomposed into phenol and CO_2 when heated quickly; ferric chloride colours the aqueous solution violet. It is an important antiseptic. It forms two series of salts (the basic calcium salt being insoluble in water), and two series of derivatives, viz.: (1) as an acid it yields chlorides, esters, &c., and (2) as a phenol it yields ethers, &c., *e.g.* ethyl-salicylic acid, $C_6H_4(O\cdot C_2H_5)CO_2H$.

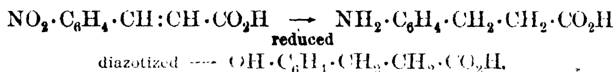
Phenyl salicylate, $C_6H_4\begin{smallmatrix}\diagup OH\\ \diagdown CO\cdot OC_6H_5\end{smallmatrix}$, the ester derived from phenol and salicylic acid, and generally termed "**Salol**", is a good antiseptic, and is prepared by the action of an acid chloride such as $POCl_3$ or $COCl_2$ upon a mixture of salicylic acid and phenol, or by heating the acid itself at 220°. It forms colourless crystals. When its sodium salt is heated to 300°, it undergoes molecular transformation into the sodium salt of the isomeric **phenyl-salicylic acid**, $C_6H_5O\cdot C_6H_4\cdot CO_2Na$ (B. **21**, 501). Analogous "salols" are obtained from other phenols, *e.g. p*-acetylaminophenol yields *salophene*.

m-**Hydroxy-benzoic acid** is prepared by diazotizing *m*-amino-benzoic acid. It crystallizes in microscopic plates, dissolves readily in hot water, and sublimes without decomposition; ferric chloride does not colour its aqueous solution.

p-**Hydroxy-benzoic acid** forms monoclinic prisms ($+ H_2O$), and ferric chloride gives no coloration with the aqueous solution. As a phenol it yields the methyl ether, anisic

acid, $C_6H_4(O \cdot CH_3) \cdot CO_2H$, which can be prepared by treating *p*-hydroxy-benzoic acid with methyl alcohol, potash and methyl iodide, and saponifying the dimethyl derivative first formed; it is also formed by the oxidation of anisole. In consequence of the phenolic hydroxyl having been etherified, it resembles the monobasic and not the phenolic acids, boiling—for example—without decomposition; hydriodic and hydrochloric acids at high temperatures decompose it into *p*-hydroxy-benzoic acid and methyl iodide or chloride.

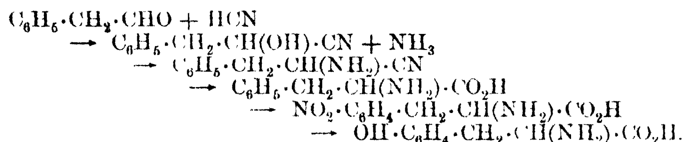
Hydro-para-coumaric acid (1:4), $OH \cdot C_6H_4 \cdot CH_2 \cdot CH_2 \cdot CO_2H$, *β-p-hydroxy-phenyl-propionic acid*, is produced by the decay of **tyrosine**, *β-hydroxy-phenyl-alanine*, $OH \cdot C_6H_4 \cdot CH_2 \cdot CH(NH_2) \cdot CO_2H$, and also synthetically from *p*-nitro-cinnamic acid:



$$NO_2 \cdot C_6H_4 \cdot CH:CH \cdot CO_2H \xrightarrow[\textbf{reduced}]{} NH_2 \cdot C_6H_4 \cdot CH_2 \cdot CH_2 \cdot CO_2H$$
$$\xrightarrow[\text{diazotized}]{} OH \cdot C_6H_4 \cdot CH_2 \cdot CH_2 \cdot CO_2H.$$

Tyrosine, which crystallizes in fine silky needles, is found in old cheese (τυρός), in the pancreatic gland, in diseased liver, in molasses, &c., and results from albumen, horn, &c., either upon boiling these with sulphuric acid or from their pancreatic digestion or their decay.

It has also been obtained synthetically, as indicated by the following series of reactions:—



$$C_6H_5 \cdot CH_2 \cdot CHO + HCN$$
$$\rightarrow C_6H_5 \cdot CH_2 \cdot CH(OH) \cdot CN + NH_3$$
$$\rightarrow C_6H_5 \cdot CH_2 \cdot CH(NH_2) \cdot CN$$
$$\rightarrow C_6H_5 \cdot CH_2 \cdot CH(NH_2) \cdot CO_2H$$
$$\rightarrow NO_2 \cdot C_6H_4 \cdot CH_2 \cdot CH(NH_2) \cdot CO_2H$$
$$\rightarrow OH \cdot C_6H_4 \cdot CH_2 \cdot CH(NH_2) \cdot CO_2H.$$

(Compare also B. **32**, 3638; Am. C. J., 1911, **45**, 368; J. C. S. 1914, **105**, 1152.)

Of the numerous **polyhydroxy-phenolic acids**, the following may be mentioned:—

Protocatechuic acid, 3:4-*Dihydroxy-benzoic acid*, is obtained by fusing various resins, such as catechu, benzoin, and kino, with alkali. It may be prepared synthetically, together with the 2:3-dihydroxy-acid, by heating catechol, $C_6H_4(OH)_2$, with ammonium carbonate. It crystallizes in glistening needles or plates, and is readily soluble in water; the solution is coloured green by ferric chloride, then—after the addition of a very little sodium carbonate—blue, and finally red. Like catechol it possesses reducing properties. Its mono-methyl ether is **vanillic**

acid, or *p-hydroxy-m-methoxy-benzoic acid*, $C_6H_3(CO_2H)(O \cdot CH_3)(OH)$, which is obtained by the oxidation of vanillin (p. 459); its dimethyl ether is the **veratric acid** of sabadilla seed (*Veratrum Sabadilla*), and its methylene ether is **piperonylic acid**, $CH_2<^{O}_{O}>C_6H_3 \cdot CO_2H$, which can be prepared, among other methods, by the oxidation of piperic acid (p. 495).

Gallic acid, 3:4:5-*Trihydroxy-benzoic acid*, $C_6H_2(OH)_3CO_2H$, occurs in nut-galls, in tea and many other plants, and as glucosides in several tannins. It is prepared by boiling tannin with dilute acids, or by allowing mould to form on its solution, and has also been obtained synthetically by various reactions. It crystallizes in fine silky needles ($+ H_2O$), dissolves readily in water, alcohol, and ether, and has a faintly acid and astringent taste. It evolves carbon dioxide readily when heated, yielding pyrogallol, reduces gold and silver salts, and yields a bluish-black precipitate with ferric chloride. Like pyrogallol, it is very readily oxidized in alkaline solution, with the production of a brown colour.

Gallic acid is used in the manufacture of blue-black inks. With ferrous sulphate it gives a pale-brown colour, which rapidly turns black on exposure to the air; the presence of a minute quantity of free sulphuric acid retards this oxidation, but when the acidified solution is used with ordinary paper the acid is neutralized by compounds present in the paper, and the oxidation takes place. Indigo carmine is added to the ink in order to give it a blue colour before oxidation occurs. *Dermatol* and *Airol* are bismuth derivatives.

Tannin is the generic name given to the naturally occurring derivatives of polyhydroxy-benzoic acids which are used for converting skins into leather. One of the most important of these is **gallotannic acid**, present in nut-galls, sumach, &c., and is a derivative of pyrogallol or gallic acid; other tanning materials appear to contain derivatives of catechol, and are often termed phlobo-tannins in contradistinction to pyrogallol tannins. They are characterized by the readiness with which they yield a red precipitate of phlobophane when their aqueous solutions are boiled with hydrochloric acid.

Some of the important tanning materials are:—Oak bark, Wattle bark, from different species of *Acacia*, *e.g. A. arabica*, *dealbata*, *decurrens* of Australia, South Africa, India; Myrabolan, the dried fruit of *Terminalia chebula* of India; Sumach (leaves of *Rhus coriaria*); Divi-divi, pod of *Caesalpina coriaria* of South

America; Cutch, extract of wood of *Acacia catechu* of India; Turwad, bark of twigs of *Cassia auriculata* of South India; Hemlock bark, Horse-chestnut bark, &c.

At one time tanners made their own infusions of extracts, but it is becoming customary to extract the material at central factories, to evaporate the aqueous extract in multiple-effect film-evaporators under reduced pressure, and to put on the market a solid extract containing very little insoluble matter and 50–60 per cent of tannins. The process of vegetable or bark tanning consists in converting the gelatine of the skin into an insoluble compound with tannin. The result is to give a durable, flexible product, which does not undergo putrefactive changes. Before tanning, the skin has to undergo several preliminary treatments, *e.g.* liming to remove hair, deliming with acid or with decomposing dung or bran, splitting into layers, &c.

Gallotannic acid is probably a penta-digalloyl derivative of glucose (cf. Glucosides, Chap. XLII, B.). All tannins are amorphous solids readily soluble in water or alcohol, but practically insoluble in ether, and yield precipitates with alkaloids, gelatins, and the salts of many heavy metals.

Quinic acid, which is found in quinine bark, coffee beans, &c., is a hexahydro-tetrahydroxy-benzoic acid, $C_6H_7(OH)_4CO_2H$. It crystallizes in colourless prisms and is optically active, an inactive modification being also known.

Thiol-benzoic acids, $SH \cdot C_6H_4 \cdot CO_2H$, are also known, and the ortho-compound readily condenses with benzene and concentrated sulphuric acid, yielding $C_6H_4\left\langle\begin{matrix}CO\\S\end{matrix}\right\rangle C_6H_4$, or with ethyl malonate or ethylacetoacetate, yielding $C_6H_4\left\langle\begin{matrix}CO\\S\end{matrix}\right\rangle CH_2$ (*Smiles* and *Ghosh*, J. C. S. 1915, **107**, 1377).

4. ALCOHOL- AND KETO-ACIDS

The monobasic aromatic alcohol-acids, which possess at one and the same time the characters of acids and of true alcohols (p. 465), contain the alcoholic hydroxyl in the side chain; this hydroxyl is consequently eliminated together with the side chain when the compound is oxidized.

In behaviour they approximate very closely to the hydroxy-acids of the fatty series, as the phenylated derivatives of which they thus appear; at the same time they yield, as phenyl

derivatives, nitro-compounds, &c., although those compounds can often not be prepared directly, on account of the readiness with which the acids are oxidized. They differ from the phenolic acids in being more soluble in water, less stable, and non-volatile; as alcohols many of them give up water and yield unsaturated acids (which the phenolic acids can never do), and they can be esterified by hydrobromic acid, &c., with the formation of halide-substitution acids, &c. Further, they are purely monobasic acids.

The hydroxy-acids may be either primary, secondary, or tertiary alcohols, *e.g.* $OH \cdot CH_2 \cdot C_6H_4 \cdot COOH$, $C_6H_5 \cdot CH \cdot (OH) \cdot COOH$, and $C_6H_5 \cdot CH_2 \cdot C(CH_3)(OH) \cdot COOH$. The tertiary can sometimes be prepared directly by the oxidation, by means of a permanganate, of such acids $C_nH_{2n-8}O_2$ as contain a tertiary hydrogen atom ($\vdots CH$).

To the ketonic acids the corresponding reactions apply. As ketones they may be reduced to secondary alcohol-acids, and they further react with hydroxylamine, &c.; as acids they form salts, esters, &c.

Mandelic acid, *Phenyl-glycollic acid*, $C_6H_5 \cdot CH(OH) \cdot CO_2H$ (1835), is formed by hydrolysing the glucoside amygdalin with hydrochloric acid, and synthetically by the hydrolysis of benzaldehyde-cyanhydrin, mandelonitrile, $C_6H_5 \cdot CH(OH) \cdot CN$ (see p. 453). It forms glistening crystals, dissolves somewhat readily in water, and melts at 133°.

Mandelic acid possesses an asymmetric carbon atom and exists in two optically active modifications (cf. B. **16**, 1565 and 2721), and these can form a racemic compound (para-mandelic acid) in the same manner as *d*- and *l*-tartaric acids.

The acid obtained synthetically is the racemic acid, but this can be resolved (1) by the aid of chinchonine when the chinchonine salt of the *d*-acid crystallizes first; (2) by means of green mould, "penicillium glaucum", which when grown on a solution of the ammonium salt of the acid destroys the lævo modification; (3) by partially esterifying the racemic acid with an optically active alcohol, *e.g.* *l*-menthol; the non-esterified acid is then *l*-rotatory, as the *d*-acid is somewhat more readily esterified by *l*-menthol than the *l*-acid. The method is not quantitative (*Marckwald* and *Mackenzie*, B. 1899, **32**, 2130; 1901, **34**, 469; also J. C. S. 1899, 964). The acid obtained from amygdalin is the lævo compound. It is comparable with lactic acid, $CH_3 \cdot CH(OH) \cdot CO_2H$, yielding, like the latter, formic acid (together with benzoic) when oxidized; hydriodic

acid reduces it to phenyl-acetic acid, just as it does lactic acid to propionic.

o-**Hydroxymethyl-benzoic acid**, $OH \cdot CH_2 \cdot C_6H_4 \cdot CO \cdot OH$, which is isomeric with mandelic acid, is unstable in the free state; as an ortho-compound, it readily yields the anhydride or lactone, **Phthalide**, $C_6H_4<\begin{matrix}CH_2\\CO\end{matrix}>O$, which is obtained by the reduction of phthalic anhydride or chloride. It crystallizes in needles or plates, and can be sublimed unaltered.

Tropic acid, *a-Phenyl-β-hydroxy-propionic acid*, $OH \cdot CH_2 \cdot CHPh \cdot CO_2H$ (fine prisms), is obtained together with tropine by boiling atropine with baryta water; it is reconverted into atropine when warmed with tropine and hydrochloric acid. It exists in *d*-, *l*-, and *r*- modifications. Tropic acid can be synthesized from ethyl phenyl-acetate and ethyl formate, which react in the presence of sodium (*Claisen* reaction), yielding ethyl formylphenylacetate, $CHO \cdot CHPh \cdot CO_2Et$, or the enolic form, $OH \cdot CH:CPh \cdot CO_2Et$, which is reduced in ethereal solution by means of aluminium amalgam to ethyl tropate (*Muller*, B. 1918, **51**, 252).

Benzoyl-formic acid, *Phenyl-glyoxylic acid*, $C_6H_5 \cdot CO \cdot CO_2H$, is obtained synthetically by the hydrolysis of benzoyl cyanide, $C_6H_5 \cdot CO \cdot CN$, with cold fuming HCl (*Claisen*, 1877), and also by the cautious oxidation of mandelic acid or acetophenone. It is an oil which only solidifies slowly, and when distilled is largely decomposed into carbon monoxide and benzoic acid. It reacts similarly to isatin with benzene containing thiophene and sulphuric acid, and shows the normal reactions of the ketonic acids with $NaHSO_3$, HCN, $NH_2 \cdot OH$, &c.

o-**Nitro-benzoyl-formic acid**, $NO_2 \cdot C_6H_4 \cdot CO \cdot CO_2H$, which can be prepared from *o*-nitro-benzoyl cyanide, yields *o*-**amino-benzoyl-formic acid**, *isatic acid*, $NH_2 \cdot C_6H_4 \cdot CO \cdot CO_2H$ (a white powder), upon reduction; when a solution of the latter is warmed, it yields its intramolecular anhydride (lactam), isatin, $C_6H_4<\begin{matrix}NH\\CO\end{matrix}>CO$ (Chap. XXXV, B.).

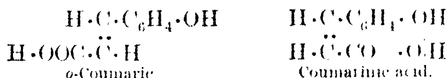
Benzoyl-acetic acid, $C_6H_5 \cdot CO \cdot CH_2 \cdot CO_2H$ (*Baeyer*), is a perfect analogue of acetoacetic acid, and, like the latter, can be used for numerous syntheses. It is obtained as its ethyl ester (which is soluble in cold sodium hydroxide solution) by dissolving ethyl phenyl-propiolate in concentrated sulphuric acid and pouring the solution into water (B. **16**, 2128); or, better, by the action of sodium ethoxide upon a mixture of

ethyl benzoate and acetate (*Claisen's* condensation, p. 233) (B. **20**, 651). It is crystalline, melts at 103°, and readily splits up into carbon dioxide and acetophenone, $C_6H_5 \cdot CO \cdot CH_3$; the aqueous solution is coloured a beautiful violet by ferric chloride.

5. UNSATURATED MONOBASIC PHENOLIC ACIDS

Hydroxy-cinnamic or **Coumaric Acids**, $OH \cdot C_6H_4 \cdot CH:CH \cdot CO_2H$.—The ortho-acid is present in melilot (*Melilotus officinalis*), and can be prepared by diazotizing *o*-amino-cinnamic acid, or from salicylic aldehyde by *Perkin's* synthesis. The alcoholic solution is yellow with a green fluorescence.

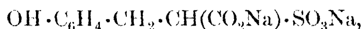
Coumarin, $C_6H_4\left\langle\begin{matrix} O-CO \\ CH:CH \end{matrix}\right.$, is the aromatic principal of woodruff (*Asperula odorata*), and is also found in the Tonquin bean and other plants. It is obtained by the elimination of water from *o*-coumaric acid by means of acetic anhydride. It crystallizes in prisms, dissolves readily in alcohol, ether, and hot water; melts at 67°, and boils at 290°. It dissolves in sodium hydroxide solution, yielding the sodium salt of **coumarinic acid**. This salt is stereo-isomeric with that of *o*-coumaric acid. The free acid itself appears to be incapable of existence, as it is immediately converted into coumarin (its anhydride), but various derivatives are known. *o*-Coumarinic acid is regarded as the *cis* compound, as it yields an anhydride (cf. Maleic Acid, p. 255). The stereo-isomeric *o*-coumaric acid is the *trans*-acid (cf. Fumaric Acid):



Synthetic coumarin is used in place of Tonquin bean and is very useful for fixing other odours. It can be synthesized by Perkin's synthesis (p. 470) from salicylaldehyde, or from *o*-chloro-benzal chloride, $Cl \cdot C_6H_4 \cdot CHCl_2$. This latter condenses with acetic acid in the presence of potassium acetate, yielding *o*-chloro-cinnamic acid, which is readily reduced to *o*-chloro-phenylpropionic acid, $Cl \cdot C_6H_4 \cdot CH_2 \cdot CH_2 \cdot CO_2H$, from which the corresponding *o*-hydroxy acid is obtained by heating with alkali. The free hydroxy acid loses water when heated, yielding **hydro-coumarin**, $C_6H_4\left\langle\begin{matrix} O \cdot CO \\ CH_2 \cdot CH_2 \end{matrix}\right\rangle$, from

which coumarin is formed by the action of bromine vapour at 270–300° (M. 1913, **34**, 1665).

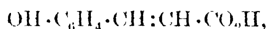
Coumarin (cis-anhydride) can be converted into coumaric (trans acid) by the following reactions. The anhydride when warmed with 20 per cent sodium bisulphite solution yields **hydro-coumarin sulphonate**, $C_6H_4\left\langle\begin{matrix} O - CO \\ CH_2\cdot\dot{C}H\cdot SO_3Na \end{matrix}\right.$, which is converted into sodium hydro-coumaric sulphonate,



$$OH\cdot C_6H_4\cdot CH_2\cdot CH(CO_2Na)\cdot SO_3Na,$$

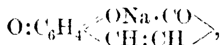
when warmed with alkali. The latter compound readily yields coumaric acid when hydrolysed (*Dodge*, J. A. C. S. 1916, **33**, 446).

Jordan and *Thorpe* (J. C. S. 1915, **107**, 396) suggest that the sodium salt of coumarinic acid, which is yellow, has the ortho-quinonoid structure, $O:C_6H_4:CH\cdot CH_2\cdot CO_2Na$, whereas the acid has the normal benzene structure



$$OH\cdot C_6H_4\cdot CH:CH\cdot CO_2H,$$

and *Dey* (*ibid.* 1622) suggests that the yellow salts of hydroxy-coumarin also have *o*- or *p*-quinone structures,



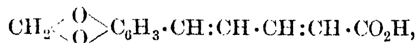
$$O:C_6H_4\left\langle\begin{matrix} ONa\cdot CO \\ CH:CH \end{matrix}\right\rangle,$$

containing quadravalent oxygen.

Coumarin derivatives can be synthesized by the condensation of ketonic esters such as ethyl aceto-acetate, ethyl benzoyl-acetate, and ethyl acetone-dicarboxylate with phenols or naphthols in the presence of sulphuric acid (*Pechmann*, B. **17**, 929, 1646, 2187; **32**, 3681; **34**, 423; *Dey*, loc. cit.).

3:4-**Dihydroxy-cinnamic acid**, *Caffeic acid*, $(OH)_2\cdot C_6H_3\cdot CH:CH\cdot CO_2H$, crystallizes in yellow prisms, and is obtained from caffetannic acid, whose mono-methyl ether is **ferulic acid** (from asafœtida); the isomeric **umbellic acid** or *p*-hydroxy-*o*-coumaric acid readily changes into the anhydride corresponding to coumarin, viz. **umbelliferone**, $C_9H_6O_3$; this last-named compound is present in varieties of Daphne.

Related to the above is **piperic acid**:



$$CH_2\left\langle\begin{matrix} O \\ O \end{matrix}\right\rangle C_6H_3\cdot CH:CH\cdot CH:CH\cdot CO_2H,$$

a decomposition product of piperine (Chap. XXXVII, B.), which crystallizes in long needles.

B. Dibasic Acids

The saturated dibasic acids of the aromatic are analogous to those of the aliphatic series, *i.e.* the acids of the oxalic series (cf. p. 239). As dibasic acids they can yield normal and acid salts, normal and acid esters, amides and amic acids, anilides and anilic acids, &c.

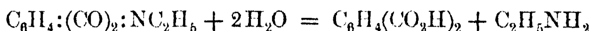
Both carboxyl groups may be attached to carbon atoms of the nucleus, or both to carbon atoms of side chains; or one attached to the nucleus and one to a side chain, *e.g.* $CO_2H \cdot C_6H_4 \cdot CH_2 \cdot CO_2H$. When the two carboxyl groups are attached to the nucleus in ortho positions, an inner anhydride of the type of succinic anhydride (p. 241) is readily formed. The isomeric meta- and para-dibasic acids do not yield such anhydrides.

Substituted dibasic acids are also known, *e.g.* hydroxy-, nitro- and amino-dibasic acids.

1. **Phthalic acid**, *Benzene-o-dicarboxylic acid*, $C_6H_4(CO_2H)_2$ (*Laurent*, 1836), is formed when any *o*-di-derivative of benzene, which contains two carbon side chains, is oxidized by HNO_3 or $KMnO_4$, but not by CrO_3 (cf. p. 467); it is generally formed by the oxidation of naphthalene by nitric acid, and also of anthracene derivatives. In preparing it on the large scale the naphthalene is first converted into its tetra-chlor-addition product, $C_{10}H_8Cl_4$, and then oxidized. At the present time phthalic acid is prepared on the commercial scale by oxidizing naphthalene with concentrated sulphuric acid in the presence of a small amount of mercury or mercuric sulphate at 220–300°. It crystallizes in short prisms or plates, melts at 213°, and is readily soluble in water, alcohol, and ether. When heated above its melting-point, it yields the anhydride. When heated with lime, it yields benzoic acid or benzene according to the relative amounts of acid and lime used. Chromic acid disintegrates it completely, while sodium amalgam converts it into dihydro-, tetrahydro-, and finally hexahydro-phthalic acid (see below). Its barium salt, $C_6H_4(CO_2)_2Ba$, is sparingly soluble in water. K = 0·121.

Phthalic anhydride, $C_6H_4 \langle {CO \atop CO} \rangle O$, crystallizes in long prisms which can be sublimed; it melts at 128°, boils at 284°, and is used in the preparation of eosin dyes (see Fluoresceïn).

Phthalimide, $C_6H_4<\substack{CO\\CO}>NH$, corresponds with succinimide in many respects. It is obtained by passing dry ammonia over heated phthalic anhydride, and readily gives rise to metallic derivatives. The *potassium salt* $C_6H_4(CO)_2NK$, obtained by the action of aqueous caustic potash on an alcoholic solution of the imide, readily reacts with alkyl iodides, yielding alkylated phthalimides, *e.g.* $C_6H_4(CO)_2NC_2H_5$, and when these are hydrolysed, primary amines, free from secondary and tertiary, are obtained, *e.g.*:



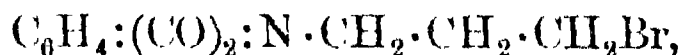
$$C_6H_4{:}(CO)_2{:}NC_2H_5 + 2H_2O = C_6H_4(CO_2H)_2 + C_2H_5NH_2$$

(*Gabriel*, B. 1887–1897). Numerous primary amines, including halogenated bases, which are difficult to prepare by other methods, have been obtained in this way. *E. Fischer* (B. 1901, **34**, 455) has also used the same method for the preparation of the complex amine ornithine,



$$NH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH(NH_2){\cdot}CO_2H,$$

$\alpha\delta$-diamino-*n*-valeric acid. The various steps are:—Potassium phthalimide and trimethylene bromide yield



$$C_6H_4{:}(CO)_2{:}N{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2Br,$$

and this on condensation with ethyl sodio-malonate gives



$$C_6H_4{:}(CO)_2{:}N{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH(CO_2Et)_2;$$

and on bromination and subsequent hydrolysis and loss of carbon dioxide $C_6H_4{:}(CO)_2{:}N{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CHBr{\cdot}CO_2H$ is obtained. Aqueous ammonia converts this into the corresponding amino-compound, and subsequent hydrolysis gives ornithine.

Ethylene and propylene oxides react with potassium phthalimide yielding compounds of the type $C_6H_4(C_2O_2){\cdot}N{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_3$, and this on hydrolysis gives β-hydroxy-*n*-propylamine, $CH_3{\cdot}CH(OH){\cdot}CH_2{\cdot}NH_2$ (*Gabriel*, B. 1917, **50**, 819).

The chloride, **phthalyl chloride**, which is obtained by the action of PCl_5 upon the acid or the anhydride, appears to have the normal constitution $C_6H_4(COCl)_2$, as it yields the compound $C_6H_4[CO{\cdot}CH(CO_2Et)_2]_2$ with ethyl sodio-malonate (*Scheiber*, A. 1912, **389**, 211; B. **45**, 2252). When heated with $AlCl_3$ it gives an isomeride which probably has the unsymmetrical formula $C_6H_4<\substack{CCl_2\\CO}>O$, as with benzene and $AlCl_3$ it yields phthalophenone, $C_6H_4<\substack{CPh_2\\CO}>O$. The symmetrical

structure for the original compound is supported by a study of its reaction with aniline, and also by the value for its molecular volume (*Ost*, A. 1912, **392**, 245). For physico-chemical study of the two forms cf. *Csanyi*, M. 1919, **40**, 81; *Ott* and *Pfeiffer*, B. 1922, 413; also Chap. XLVII, E.

2. **Isophthalic acid** (1:3), prepared from *m*-xylene, crystallizes in slender needles from hot water, in which it is only sparingly soluble; it sublimes without forming an anhydride. The barium salt is readily soluble in water. K = 0·0287.

Uvitic acid is 5-methyl-isophthalic acid, and may be obtained by oxidizing mesitylene.

3. **Terephthalic acid** (1:4) is obtained by the oxidation of *p*-xylene, cymene, &c., and especially of oil of turpentine or oil of cumin. It forms a powder almost insoluble in alcohol and water, and sublimes unchanged. For its preparation *p*-toluic acid is oxidized by potassic permanganate (A. **258**, 9). The barium salt is only sparingly soluble.

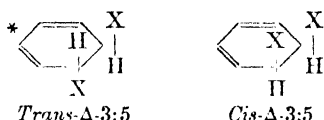
A. Baeyer's researches (A. 245, 251, 258, 266, 269, and **276**) have introduced us to a whole series of reduction products of phthalic acid, generally known as hydro-phthalic acids. The isomers among them differ from one another either by the position of the double bond in the ring (*structural isomerism*), or by the spatial arrangement of the carboxyl groups with respect to the ring (*stereo-isomerism*). This latter isomerism corresponds to a certain extent with that of fumaric and maleic acids, but more closely with that of the poly-methylene compounds (p. 350), and a distinction is therefore made here also between a *trans*- and a *cis*-form (cf. A. **245**, 130). Exactly the same applies to the hydro-terephthalic acids.

Of the **hydro-phthalic acids** (A. 269, 147) there are now known:—Five *dihydro-acids* (two of which are stereo-isomeric), four *tetrahydro-acids* (of which two again are stereo-isomeric), and two *hexahydro-acids* (which are stereo-isomers). Of the **hydro-terephthalic acids** (A. **258**, 1), five *dihydro-*, three *tetrahydro-*, and two *hexahydro-acids* are known, two in each group being stereo-isomeric.

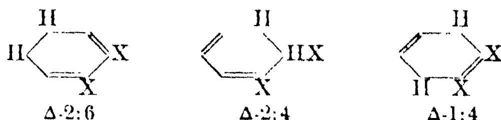
The following principles have largely served for determining the position of the double bonds in these compounds:—(1) When bromine substitutes in a carboxylic acid it takes up the α-position to the carboxyl (*i.e.* it is attached in the benzene nucleus to the same carbon atom to which the carboxyl is linked). (2) If two bromine atoms stand in the *ortho*-position to one another in a reduced benzene nucleus, they are elimi-

nated, without replacement, by the action of zinc dust and glacial acetic acid; whereas, if they stand in the *para*-position, they are replaced by hydrogen. (3) As in the case of the aliphatic unsaturated acids, boiling with sodic hydroxide solution often gives rise to an isomeric acid, due to the "wandering" of a double bond in the direction of a carboxyl group (p. 168). (4) The stereo-isomeric modifications are also easily transformed one into the other.

The relations existing between the five known dihydrophthalic acids may be taken as an example. When phthalic acid is reduced by sodium amalgam in presence of acetic acid, *trans*-Δ-3:5-dihydro-phthalic acid is produced, and this changes into the *cis*-Δ-3:5-acid when heated with acetic anhydride:



Both of these yield the Δ-2:6-dihydro-acid when warmed with alkali. When the dihydrobromide of the latter acid is treated with alcoholic potash, the Δ-2:4-dihydro-acid results, and, lastly, the anhydride of this yields the anhydride of the Δ-1:4-dihydro-acid when heated:



All the dihydro-phthalic acids give anhydrides with the exception of the *trans*-Δ-3:5-acid, which in this respect comports itself like fumaric acid.

The following relationships have been established between the hydro-terephthalic acids:—

Terephthalic acid reduced with pure sodium amalgam in faintly alkaline solution gives a mixture of *cis*- and *trans*-Δ-2:5-dihydro-acids, both of which on oxidation readily yield terephthalic acid. When boiled with water both are converted into the Δ-1:5-dihydro-acid, and when boiled with caustic soda

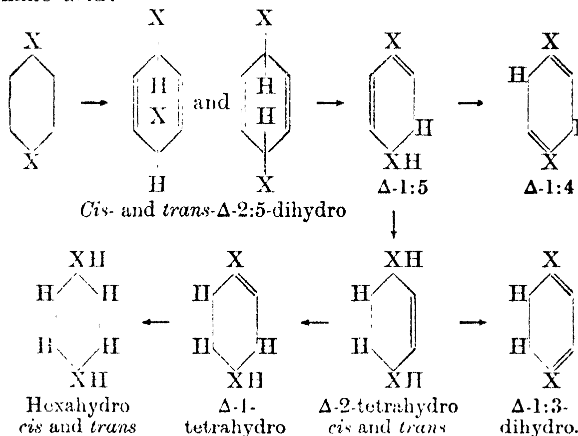
* In these formulæ $X = CO_2H$, Δ denotes the double bond, and the numbers refer to the carbon atoms after which the double bonds are placed. Δ-3:5 indicates two double bonds, one between carbons 3 and 4, and a second between carbons 5 and 6.

solution into the Δ-1:4-dihydro-acid. This acid is the most stable of the dihydro-acids, and is always obtained by the reduction of terephthalic acid unless great care is taken.

When reduced with sodium amalgam the Δ-1:5-acid is converted into a mixture of *cis-* and *trans*-Δ-2-tetrahydro-acids, which are also formed when the original acid is reduced with **pure** sodium amalgam (B. 1928, 871). Both acids readily combine with bromine, which can again be removed by means of zinc dust; this dibromide, when warmed with alcoholic potash, gives the Δ-1:3-dihydro-acid, which cannot be obtained directly by the reduction of terephthalic acid.

The Δ-1-tetrahydro-acid may be obtained by warming the Δ-2-acid with sodium hydroxide solution.

The Δ-1-acid yields a mixture of two stereo-isomeric dibromides (*cis* and *trans*), and these when reduced with zinc dust and acetic acid yield the *cis-* and *trans*-hexahydro-terephthalic acid:



The completely hydrogenized acids show great differences from the partially hydrogenized. Thus, hexahydro-terephthalic acid is exactly similar to a saturated acid of the fatty series, cold permanganate of potash has no effect upon it, while bromine substitutes (upon warming).

On the other hand, the partially hydrogenized acids comport themselves precisely like the unsaturated acids of the fatty series with an open chain. They are very readily oxidized by cold permanganate, and take up bromine or hydrobromic

acid until the saturation stage of the hexa-methylene ring is reached. All of the hydro-acids can be transformed back into phthalic acid (A. 1894, **280**, 94).

For **hydro-isophthalic acids**, see *W. H. Perkin, Jun.*, and *S. S. Pickles*, P. 1905, 75, and *Baeyer* and *Villiger*, A. 1893, **276**, 255. Two stereo-isomeric modifications of the hexahydro-acid are also obtained synthetically from derivatives of the fatty series (*Perkin*, J. C. S. 1891, 798). This constitutes a further proof that the hexahydro-benzene-carboxylic acids are nothing more than hexa-methylene derivatives.

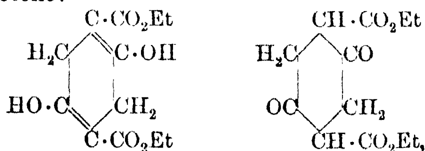
A large number of substitution products of the phthalic acids are known, *e.g.* chloro- and **bromo-phthalic acids** (which are used in the eosin industry), nitro-, amino-, hydroxy- and sulpho-phthalic acids, &c.

HYDROXY-PHTHALIC ACIDS

2·5-**Dihydroxy-terephthalic acid**, *quinol-p-dicarboxylic acid*, $C_6H_2(OH)_2(CO_2H)_2$, in which both the hydroxyls and the carboxyls are respectively in the *p*-position to one another, is obtained as its ethyl ester by the action of bromine upon succinylo-succinic ester, or of sodium ethoxide upon dibromo-acetoacetic ester. The free acid breaks up into quinol and carbon dioxide when distilled, and is converted by nascent hydrogen into succinylo-succinic acid.

Succinylo-succinic acid, *p-dihydroxy-dihydro-terephthalic acid*, $C_6H_4(OH)_2(CO_2H)_2$, is obtained as its ethyl ester by the action of sodium upon ethyl succinate (see p. 371). The **ethyl ester** crystallizes in triclinic prisms which melt at 126°, and dissolves in alcohol to a bright-blue fluorescent liquid which is coloured cherry-red by ferric chloride. It contains two replaceable hydrogen atoms, being analogous to acetoacetic ester. The free acid, on losing carbon dioxide, changes into tetrahydro-quinone or *p-diketo-hexamethylene*.

The ester may be represented as a dihydroxylic compound or as a diketone:



and reacts as a tautomeric substance (cf. Ethyl Acetoacetate).

C. Polybasic Acids

Benzene *s*-tricarboxylic acid or **trimesic acid**, $C_6H_3(COOH)_3$, can be obtained by the oxidation of mesitylene. The isomeric unsym. acid or **trimellitic acid** is obtained by the oxidation of colophonium, and the adjacent acid or **hemimellitic acid** is obtained by oxidizing naphthalene-1:8-dicarboxylic acid.

The benzene tetracarboxylic acids, $C_6H_2(CO_2H)_4$, **prehnitic acid** [1:2:3:4], **mellophanic acid** [1:2:3:5], and **pyromellitic acid** [1:2:4:5], are obtained by heating mellitic acid or its hexahydro-derivatives.

Mellitic acid, $C_6(CO_2H)_6$, occurs in peat as aluminium salt or honey-stone, $C_{12}Al_2O_{12} + 18H_2O$, which crystallizes in octahedra, and is also formed by the oxidation of lignite or graphite with $KMnO_4$. It forms fine silky needles of great stability, can neither be chlorinated, nitrated, nor sulphonated, but is readily reduced by sodium amalgam to **hydromellitic acid**, $C_6H_6(CO_2H)_6$, and yields benzene when distilled with lime.

As regards the esterification of these polybasic acids, it has been found that carboxylic groups which have other carboxylic groups in two ortho-positions cannot be esterified by the usual catalytic process, *e.g.* on esterification by the *Fischer-Speyer* method, hemimellitic acid and prehnitic acid yield dimethyl esters only, pyromellitic acid yields a tetramethyl ester, and mellitic acid is not acted on (*V. Meyer* and *Sudborough*, B. 1894, **27**, 3146).

XXVII. AROMATIC COMPOUNDS CONTAINING TWO OR MORE BENZENE NUCLEI. DIPHENYL GROUP.

The aromatic compounds hitherto considered, with the exception of azobenzene, benzophenone, &c., contain but one benzene nucleus. In addition to these, however, a considerable number of compounds are known which contain two or more such nuclei united in a variety of ways. Such compounds are usually arranged in the following groups :—

1. **Diphenyl group** ; this comprises the compounds with two benzene nuclei directly united together. The parent substance of the group is diphenyl, $C_6H_5 \cdot C_6H_5$.

2. **Diphenyl-methane group** ; this includes all compounds with two benzene nuclei attached to a single carbon atom.

The parent substance is diphenyl-methane, $C_6H_5 \cdot CH_2 \cdot C_6H_5$.

3. **Dibenzyl or stilbene group**, which comprises compounds containing two benzene nuclei linked together by a chain of two or more carbon atoms, *e.g.* dibenzyl, $C_6H_5 \cdot CH_2 \cdot CH_2 \cdot C_6H_5$, and stilbene, $C_6H_5 \cdot CH{:}CH \cdot C_6H_5$.

4. **Triphenyl-methane group**, which contains the compounds with three benzene nuclei attached to a single carbon atom, *e.g.* triphenyl-methane, $CH(C_6H_5)_3$.

5. In addition to the above groups several extremely important groups are known which contain two or more benzene nuclei arranged in such a manner that they have two or more carbon atoms in common (see naphthalene and anthracene).

DIPHENYL GROUP

Diphenyl is related to benzene in much the same manner as ethane to methane:



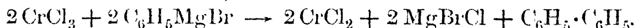
$$CH_4 \text{ and } CH_3 \cdot CH_3 \qquad C_6H_6 \text{ and } C_6H_5 \cdot C_6H_5.$$

Its molecule consists of two benzene nuclei directly united. Its method of synthesis by *Fittig*, by the action of sodium on an ethereal solution of monoiodo-benzene or of copper-bronze at 230° (*Ullmann*, A. **332**, 38), is analogous to the formation of ethane by the action of zinc or sodium on methyl iodide:



$$2C_6H_5I + 2Cu = C_6H_5 \cdot C_6H_5 + Cu_2I_2.$$

An interesting synthesis is from phenyl magnesium bromide and anhydrous $CrCl_3$ or $CuCl_2$; in both cases the metallic chloride is reduced to the lower 'ous form (J. C. S. 1914, **105**, 1057; 1919, **115**, 559):



$$2\,CrCl_3 + 2\,C_6H_5MgBr \longrightarrow 2\,CrCl_2 + 2\,MgBrCl + C_6H_5 \cdot C_6H_5.$$

Another synthesis is from *p*-di-iodo-benzene and magnesium. The mono- and di-magnesium compounds are first formed, and these react, yielding $IMg \cdot C_6H_4 \cdot C_6H_4 \cdot MgI$, which is converted into di-phenyl by the action of water (B. 1914, **47**, 1219):



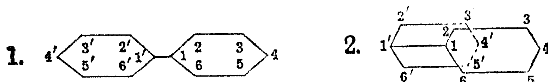
$$C_6H_4I_2 \longrightarrow IC_6H_4 \cdot MgI + IMg \cdot C_6H_4 \cdot MgI \longrightarrow MgI_2 + IMg \cdot C_6H_4 \cdot C_6H_4 \cdot MgI.$$

It is also formed by passing the vapour of benzene through a red-hot tube. It is contained in coal-tar, crystallizes in large colourless plates, melts at 71°, boils at 254°, and is readily soluble in alcohol and ether.

Chromic acid oxidizes diphenyl to benzoic acid, one of the two benzene nuclei being destroyed. From this and from

its synthesis, the formula of diphenyl must be $C_6H_5 \cdot C_6H_5$.

Derivatives (*Schultz*, A. **207**, 311).—Like benzene, diphenyl is the mother substance of a series of derivatives which closely resemble the corresponding benzene derivatives. With poly-substituted derivatives the substituents are usually denoted by the following numbers, according to the position occupied:



Mono-substituted derivatives exist in *o*-, *m*-, or *p*-forms, according to the position of the substituent with reference to the point of union of the two nuclei. The number of di-substituted derivatives is still larger. The constitution of these is elucidated from their syntheses, from their products of oxidation, or by conversion into compounds of known constitution; thus a chloro-diphenyl, $C_{12}H_9Cl$, which yields *p*-chloro-benzoic acid when oxidized by chromic acid, is obviously *p*-chloro-diphenyl. Whether all the substituents are attached to the one nucleus or are distributed between the two, can also be proved by an examination of the products of oxidation.

The substituents take up the *p*-position for choice; in di-derivatives the *p*-*p*- (and to a lesser extent the *o*-*p*-) position.

The spatial arrangement of the diphenyl molecule has attracted attention. *Kaufler* (A. 1907, **351**, 151) has suggested that the two benzene nuclei lie in parallel planes and are not free to rotate around the axis joining the two nuclei (No. 2).

All the known facts, however, are readily explicable by means of the simpler formula 1, according to which the two nuclei lie in the same plane and their two axes in a straight line. A slightly modified structure has to be adopted for certain 2 : 6 : 2′ : 6′ substituted derivatives which can exist in optically active forms (see Chap. XLVI, A.).

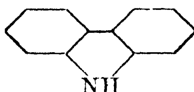
Di-*p*-diamino-diphenyl, *benzidine*, $NH_2 \cdot C_6H_4 \cdot C_6H_4 \cdot NH_2$ (*Zinin*, 1845), is obtained by the reduction of *p*-*p*-dinitro-diphenyl (the direct nitration product of diphenyl); also, together with diphenyline, by the action of acids upon hydrazobenzene, the latter undergoing a molecular transformation (p. 423): $C_6H_5 \cdot NH \cdot NH \cdot C_6H_5 \rightarrow NH_2 \cdot C_6H_4 \cdot C_6H_4 \cdot NH_2$; it is consequently formed directly from azobenzene by treating it with tin and hydrochloric acid.

Benzidine is a diacid base which crystallizes in colourless silky plates, is readily soluble in hot water or alcohol, and

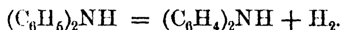
melts at 122°. Its **sulphate**, $C_{12}H_{10}(NH_2)_2 \cdot SO_4H_2$, is sparingly soluble. Like its homologues (tolidine, &c.), it is of special importance in the colour industry, as its diazonium-compound couples with naphthol-sulphonic or naphthylamine-sulphonic acids, yielding the "substantive" or cotton dyes (cf. Chap. LV).

The isomeric **diphenyline**, 2:4′-diamino-diphenyl, may be obtained from 2:4′-dinitro-diphenyl, and also as a by-product in the preparation of benzidine from azobenzene. It crystallizes in needles, melting at 45°, and yields a sulphate which is readily soluble.

Carbazole,



the imide of diphenyl, is contained in coal-tar and in crude anthracene. It is formed by distilling *o*-amino-diphenyl over lime at a low red heat, or by passing the vapour of diphenylamine through red-hot tubes, just as diphenyl is obtained from benzene:



$$(C_6H_5)_2NH = (C_6H_4)_2NH + H_2.$$

It crystallizes in colourless plates sparingly soluble in cold alcohol, melts at 238°, distils unchanged, and is characterized by the readiness with which it sublimes. Concentrated sulphuric acid dissolves it to a yellow solution, and it forms an acetyl- and a nitro-compound, &c. The nitrogen in it occupies the di-ortho-position; it thus appears, like indole, to be a pyrrole derivative, and it shows, in fact, most striking analogies to the latter (B. **21**, 3299).

Benzidine-mono-, di-, &c. sulphonic acids, *e.g.* $C_{12}H_6(NH_2)_2(SO_3H)_2$, are of technical importance. The **dihydroxy-diphenyls**, $C_{12}H_8(OH)_2$, of which four isomers are known, are formed (*a*) by diazotizing benzidine, (*b*) by fusing diphenyl-disulphonic acid with potash, and (*c*) by fusing phenol with potash or by oxidizing it with permanganate; in the last case hydrogen is separated and two benzene residues join together.

Diphenylene oxide, $\begin{matrix}C_6H_4 \\ \cdot \\ C_6H_4\end{matrix}\!\!>\!O$, is obtained by distilling phenol with plumbous oxide; it crystallizes in plates which distil without decomposition (cf. *e.g.* B. **25**, 2745).

The **carboxylic acids** of diphenyl are obtained (1) from the

corresponding nitriles, which on their part are prepared by distilling the sulphonic acids of diphenyl with KCN, *e.g.* **di-*p*-diphenyl-dicarboxylic acid**, $C_{12}H_8(CO_2H)_2$, a white powder insoluble in water, alcohol, and ether; (2) by the oxidation of phenanthrene and similar compounds, *e.g.*, **diphenic acid**, $CO_2H \cdot C_6H_4 \cdot C_6H_4 \cdot CO_2H$, the 2:2′-dicarboxylic acid, crystallizing in needles or plates which are readily soluble in the solvents just mentioned; m.-pt. 229°. Both of these are dibasic acids, which yield diphenyl when heated with soda-lime.

The homologues of diphenyl are, like the latter, obtained by means of *Fittig's* reaction. Analogous to benzidine is *o*-**tolidine**, $C_{12}H_6(CH_3)_2(NH_2)_2$, m.-pt. 128°, similarly **dianisidine, dimethoxy-benzidine**, $C_{12}H_6(O \cdot CH_3)_2(NH_2)_2$. All these compounds yield diazonium salts, which couple with naphthols and then sulphonic acids to form substantive dyes. (Chap. LV.)

Diphenyl may be regarded as monophenyl-benzene; the corresponding di- and triphenyl-benzenes are also known.

p-**Diphenyl-benzene**, $C_6H_4(C_6H_5)_2$, may be obtained by the action of sodium upon a mixture of *p*-dibromo-benzene and bromo-benzene. It crystallizes in flat prisms, melts at 205°, and on oxidation yields diphenyl-monocarboxylic and terephthalic acids.

When hydrochloric acid gas is led into acetophenone, $C_6H_5 \cdot CO \cdot CH_3$, a reaction analogous to the formation of mesitylene from acetone (p. 369) ensues, and *s*-**triphenyl-benzene**, $C_6H_3(C_6H_5)_3$ (rhombic plates), is formed.

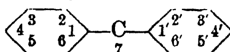
XXVIII. DIPHENYL-METHANE GROUP

Diphenyl-methane, $C_6H_5 \cdot CH_2 \cdot C_6H_5$, is derived from methane by the replacement of two hydrogen atoms by two phenyl groups, and is thus closely related to phenyl-methane or toluene, $C_6H_5 \cdot CH_3$. One important difference is that when oxidized it cannot yield an acid containing the same number of carbon atoms since it does not contain a methyl group. It can be oxidized to the secondary alcohol benzhydrol, $(C_6H_5)_2CH \cdot OH$, or the ketone benzophenone, $(C_6H_5)_2CO$. Compounds like diphenyl-ethane, $(C_6H_5)_2CH \cdot CH_3$, can yield acids.

The various derivatives are obtained by substituting one

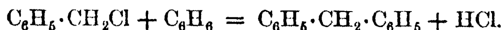
or more of the twelve hydrogen atoms present in the diphenyl-methane molecule. If the substituent replaces any of the ten hydrogens directly attached to the benzene nuclei, a compound is formed which closely resembles the corresponding derivatives of benzene, *e.g.* $C_6H_5 \cdot CH_2 \cdot C_6H_4 \cdot NH_2$ closely resembles aniline. If, on the other hand, the substituent replaces a hydrogen atom of the methylene group, a compound with aliphatic properties is obtained, *e.g.* $(C_6H_5)_2CH \cdot OH$ closely resembles a secondary aliphatic alcohol.

The method of numbering the carbon atoms in the diphenyl-methane molecule is usually as follows:—



Formation of diphenyl-methane and its derivatives.

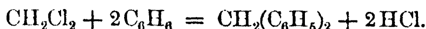
1. Diphenyl-methane is produced by the action of benzyl chloride upon benzene, in presence of zinc dust (*Zincke*, A. **159**, 374), or of aluminium chloride (*Friedel* and *Crafts*):



$$C_6H_5 \cdot CH_2Cl + C_6H_6 = C_6H_5 \cdot CH_2 \cdot C_6H_5 + HCl.$$

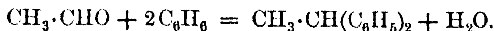
The homologues of benzene, and also the phenols and tertiary amines, may be used instead of benzene itself.

In an exactly analogous manner diphenyl-methane is obtained by the action of methylene chloride, CH_2Cl_2, upon benzene in presence of aluminium chloride:



$$CH_2Cl_2 + 2C_6H_6 = CH_2(C_6H_5)_2 + 2HCl.$$

2. Diphenyl-methane hydrocarbons are formed by the action of the aliphatic aldehydes, *e.g.* acetaldehyde or formaldehyde, upon benzene, &c., in the presence of concentrated sulphuric acid (*Baeyer*, B. 6, 963). With formaldehyde diphenyl-methane, or with acetaldehyde diphenyl-ethane, is formed:



$$CH_3 \cdot CHO + 2C_6H_6 = CH_3 \cdot CH(C_6H_5)_2 + H_2O.$$

The acetaldehyde and formaldehyde are employed here in the form of paraldehyde and methylal. Formaldehyde itself condenses with aniline to diamino-, and with dimethyl-aniline to tetramethyl-diamino-diphenyl-methane. When aromatic aldehydes are used, triphenyl-methane derivatives are formed (p. 512).

3. Aromatic alcohols react with benzene and sulphuric acid in an analogous manner (*V. Meyer*):



$$C_6H_5 \cdot CH_2 \cdot OH + C_6H_6 = C_6H_5 \cdot CH_2 \cdot C_6H_5 + H_2O.$$

Similar reactions have also been brought about by means of ketones, aldehydo-acids, and keto-acids on the one hand, and phenol and dialkylated anilines on the other.

The true aromatic ketones of the type of benzophenone may be regarded as diphenyl-methane derivatives (see p. 458).

Diphenyl-methane, $(C_6H_5)_2CH_2$, is most conveniently prepared from benzyl chloride, benzene, and aluminium chloride. It crystallizes in colourless needles of very low melting-point (26°), is readily soluble in alcohol and ether, has a pleasant odour of oranges, and distils unaltered at 262°.

It yields nitro-, amino-, and hydroxy-derivatives. *p*-**Diamino-diphenyl-methane,** $CH_2(C_6H_4NH_2)_2$, is obtained by heating methylene-aniline, $C_6H_5{\cdot}N{:}CH_2$, prepared from formaldehyde and aniline, with aniline and an aniline salt. It crystallizes in lustrous silvery plates, melting at 87°, and may be used for the preparation of fuchsine. Bromine at a moderate temperature reacts with the hydrocarbon yielding **diphenyl-bromo-methane,** $(C_6H_5)_2CHBr$, and when this is heated with water to 150°, it yields **benzhydrol,** *diphenyl-carbinol*, $(C_6H_5)_2CH{\cdot}OH$, which can also be obtained from benzophenone and sodium amalgam, or by *Grignard's* synthesis from benzaldehyde and phenyl magnesium bromide (C. R. 1914, **158**, 534). It crystallizes in glistening silky needles, melts at 68°, possesses in every respect the character of a secondary alcohol (forming esters, amines, &c.), and is readily oxidized to the corresponding ketone, benzophenone, $(C_6H_5)_2CO$ (p. 458).

aa-**Diphenyl-ethane,** $(C_6H_5)_2CH{\cdot}CH_3$ (isomeric with dibenzyl, see p. 509), is obtained by method of formation 2 (p. 507). It is a liquid, boils at 286°, and is oxidized to benzophenone by chromic acid. From it is derived:

Benzilic acid, *diphenyl-glycollic acid*, $(C_6H_5)_2C(OH){\cdot}CO_2H$, which is formed by a molecular transformation when benzil, $C_6H_5{\cdot}CO{\cdot}CO{\cdot}C_6H_5$ (p. 511), is fused with potash. It crystallizes in needles or prisms, dissolves in concentrated sulphuric acid to a blood-red solution, and is reduced by hydriodic acid to **diphenyl-acetic acid,** $(C_6H_5)_2CH{\cdot}CO_2H$ (needles or plates), which may also be obtained synthetically from phenyl-brom-acetic acid, $C_6H_5{\cdot}CHBr{\cdot}CO_2H$, benzene, and zinc dust, according to mode of formation 1, p. 507.

Benzoyl-benzoic acids, benzophenone-carboxylic acids, $C_6H_5{\cdot}CO{\cdot}C_6H_4{\cdot}CO_2H$ (B. **6**, 907). Of these the *o*-acid (m.-pt. 127°) has been prepared synthetically by heating phthalic anhydride

with benzene and aluminium chloride. When heated with phosphorus pentoxide at 180°, it yields anthra-quinone, $C_6H_4<\substack{CO\\CO}>C_6H_4$; various transformations into the anthracene series have been effected in a similar manner from *o*-tolyl-phenyl-methane and the corresponding ketone.

Fluorene, *diphenylene-methane*, $\begin{matrix}C_6H_4\\ \cdot\\ C_6H_4\end{matrix}>CH_2$, stands in the same relation to diphenyl-methane as carbazole (p. 505) does to diphenylamine; it is at the same time a diphenyl and a methane derivative. It is contained in coal-tar, and is produced when diphenyl-methane is led through red-hot tubes (like diphenyl from benzene), and also by passing the vapour of diphenylene-ketone over red-hot zinc dust. It crystallizes in colourless plates with a violet fluorescence, melts at 113°, and boils at 295°. The corresponding ketone, **diphenylene-ketone**, $C_{12}H_8:CO$, which crystallizes in yellow prisms melting at 84°, is obtained by heating phenanthra-quinone with lime, and is converted into **fluorenyl alcohol**, $(C_6H_4)_2:CH\cdot OH$ (colourless plates, m.-pt. 153°), by nascent hydrogen, and into **diphenyl-carboxylic acid, *o*-phenyl-benzoic acid**, $C_6H_5\cdot C_6H_4\cdot CO_2H$, by fusion with potash.

XXIX. DIBENZYL GROUP

This group comprises the compounds containing two benzene nuclei connected by a chain of two carbon atoms. Among the most important members are:—Dibenzyl, $C_6H_5\cdot CH_2\cdot CH_2\cdot C_6H_5$; stilbene, $C_6H_5\cdot CH:CH\cdot C_6H_5$; tolane, $C_6H_5\cdot C:C\cdot C_6H_5$; deoxybenzoin, $C_6H_5\cdot CH_2\cdot CO\cdot C_6H_5$; hydrobenzoin, $C_6H_5\cdot CH(OH)\cdot CH(OH)\cdot C_6H_5$; benzoin, $C_6H_5\cdot CH(OH)\cdot CO\cdot C_6H_5$; benzil, $C_6H_5\cdot CO\cdot CO\cdot C_6H_5$.

Dibenzyl is symmetrical diphenyl-ethane (for the unsymmetrical compound, see p. 508), stilbene is *s*-diphenyl-ethylene, and tolane diphenyl-acetylene.

All these compounds yield benzoic acid when oxidized.

Dibenzyl is formed when benzyl chloride is treated with metallic sodium, or by the action of benzyl chloride on benzyl magnesium chloride. It is often met with as a by-product in *Grignard's* synthesis by means of benzyl magnesium chloride.

It is isomeric with ditolyl and with tolyl-phenyl-methane; it crystallizes in needles or small plates, melts at 52°, and sublimes unchanged.

Stilbene, *s-diphenyl-ethylene*, forms monoclinic plates or prisms, melts at 125°, and also boils without decomposition. It may be prepared by the action of sodium upon benzal chloride, or by heating deoxybenzoïn with sodium ethoxide, or best by the action of benzyl magnesium chloride on benzaldehyde, and possesses the full character of an olefine, giving, for instance, a dibromide, $C_6H_5 \cdot CHBr \cdot CHBr \cdot C_6H_5$, with bromine, and being converted into dibenzyl by hydriodic acid. *p*-**Diamino-stilbene**, $C_{14}H_{10}(NH_2)_2$, and its disulphonic acid (obtained by reducing *p*-nitro-toluene or its sulphonic acid in alkaline solution) are, like benzidine, mother substances of "substantive dyes" (Chap. LV, B.). Stilbene should exist in two stereo-isomeric modifications, the ordinary stilbene melting at 125° is usually regarded as the *trans* compound $\begin{matrix} H \cdot C \cdot Ph \\ \cdot\cdot \\ Ph \cdot C \cdot H \end{matrix}$.
An isomeride—the *cis* compound has been described by *Otto* and *Stoffel* (B. 1897, **30**, 1799). Just as ethylene bromide yields acetylene when boiled with alcoholic potash, so stilbene dibromide yields **tolane**, which crystallizes in prisms or plates, melting at 60°. It may also be prepared by the following series of reactions:—

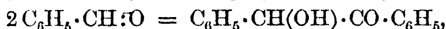

$C_6H_5 \cdot CH_2 \cdot CO \cdot C_6H_5 \xrightarrow{\text{Phosphorus pentachloride}} C_6H_5 \cdot CH : CCl \cdot C_6H_5 \xrightarrow{\text{Alcoholic potash}} C_6H_5 \cdot C \vdots C \cdot C_6H_5$.

Tolane corresponds with acetylene in its properties in so far that it combines with chlorine to a dichloride and a tetrachloride; but it does not yield metallic derivatives, since it contains no "acetylene hydrogen" (p. 54).

When stilbene dibromide is treated with silver acetate, two di-acetates are formed; and when these are hydrolysed by alcoholic ammonia, two isomeric substances of the composition, $C_6H_5 \cdot CH(OH) \cdot CH(OH) \cdot C_6H_5$, **hydrobenzoïn** and **iso-hydrobenzoïn** or *s-diphenyl-glycol*, are produced. Both compounds are also formed by the action of sodium amalgam upon oil of bitter almonds. The former crystallizes in rhombic plates, melting at 138°, and the latter in four-sided prisms, melting at 119°, and is the more soluble of the two. The two compounds are stereo-isomeric in the same manner as meso-tartaric and racemic acid, and *Erlenmeyer*, *Junr.*, has been able to resolve hydrobenzoïn, which corresponds with racemic acid, into

two optically active components, by separating two different kinds of hemihedral crystals (A. **198**, 115, 191; B. **30**, 1531).

The compounds **benzoïn, benzil,** and **deoxybenzoïn,** which have already been mentioned, are closely related to one another, as their formulæ show, and can also be prepared from benzaldehyde. When the aldehyde is boiled with an alcoholic solution of potassium cyanide it polymerises,* yielding benzoïn,



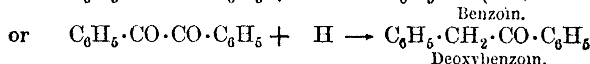
$$2\,C_6H_5{\cdot}CH{:}O = C_6H_5{\cdot}CH(OH){\cdot}CO{\cdot}C_6H_5,$$

which forms beautiful glistening prisms, m.-pt. 134°; nascent hydrogen reduces it to hydrobenzoïn, from which it can also be obtained by oxidation. It reduces *Fehling's* solution even at the ordinary temperature, yielding benzil.

Benzil, $C_6H_5{\cdot}CO{\cdot}CO{\cdot}C_6H_5$, is obtained by oxidizing benzoin with nitric acid. It crystallizes in large six-sided prisms, melting at 95°. It is oxidized to benzoic acid by chromic anhydride, and reduced by nascent hydrogen—according to the conditions—either to benzoin or to deoxybenzoïn,



$$C_6H_5{\cdot}CO{\cdot}CO{\cdot}C_6H_5 + 2\,H \longrightarrow \underset{\text{Benzoin.}}{C_6H_5{\cdot}CH(OH){\cdot}CO{\cdot}C_6H_5}$$



or $$C_6H_5{\cdot}CO{\cdot}CO{\cdot}C_6H_5 + H \longrightarrow \underset{\text{Deoxybenzoin.}}{C_6H_5{\cdot}CH_2{\cdot}CO{\cdot}C_6H_5}$$

It reacts with hydroxylamine to produce:

Benzil-monoxime, $C_6H_5{\cdot}CO{\cdot}C({:}N{\cdot}OH){\cdot}C_6H_5$, and **benzil-dioxime,** $C_6H_5{\cdot}C({:}N{\cdot}OH){\cdot}C({:}N{\cdot}OH){\cdot}C_6H_5$, which exist in the following stereo-isomeric modifications (*Hantzsch* and *Werner*, B. **23**, 11; **37**, 4295; *Dittrich, ibid.*, **24**, 3267):—

Monoximes:

α. M.-pt. 134°, β. M.-pt. 113°.

Dioximes:

α. M.-pt. 237°, β. M.-pt. 207°, γ. M.-pt. 163°, and possibly a fourth form.

For discussion on configurations, see Chap. XLVI, C.

Deoxybenzoïn, $C_6H_5{\cdot}CH_2{\cdot}CO{\cdot}C_6H_5$, forms large plates, melting at 55°, and may be sublimed or distilled unchanged. It can be prepared by the action of benzene and aluminium chloride upon phenyl-acetyl chloride, $C_6H_5{\cdot}CH_2{\cdot}CO{\cdot}Cl$, and hence its constitution, and yields di-benzyl with hydriodic acid. Deoxybenzoïn can also be prepared from benzil and benzoïn (B. **25**, 1728). One of its methylene hydrogen atoms

* For mechanism, cf. *Chalanay* and *Knoevenagel* (B. 1892, **25**, 295).

is readily replaceable by alkyl, just as in acetoacetic ester. The radical, $CH(C_6H_5)\cdot CO\cdot C_6H_5$, is termed "desyl".

Benzilic acid, $(C_6H_5)_2C(OH)\cdot CO_2H$ (p. 508), is produced when benzil is heated with alcoholic potash, by a peculiar molecular transformation similar to that by which pinacoline is formed (p. 200).

Compounds closely related to the dibenzyl group are those which contain two benzene nuclei united by a chain of more than two carbon atoms, *e.g.* αγ-diphenyl propane, and also those compounds containing three or more benzene nuclei united by a chain of carbon atoms, *e.g.* triphenyl-ethane, tetraphenyl-ethane, &c.

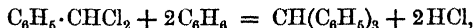
XXX. TRIPHENYL-METHANE GROUP

Triphenyl-methane, $CH(C_6H_5)_3$, is the compound obtained as the result of the entrance of three phenyl groups into the methane molecule; among its homologues are tolyl-diphenyl-methane, $(C_6H_5)_2CH\cdot C_6H_4\cdot CH_3$, ditolyl-phenyl-methane, $C_6H_5\cdot CH(C_6H_4\cdot CH_3)_2$, &c.

These hydrocarbons are of especial interest as being the mother substances of an extensive series of dyes; the amino-, hydroxy-, and carboxy-derivatives of triphenyl-methane are the leuco-bases obtained from such dyes as rosaniline, aurine, malachite green, &c.

Their *formation* is effected in a manner analogous to that of the diphenyl-methane derivatives, *i.e.* by the aid of zinc dust or aluminium chloride when chlorine compounds are used, or by the aid of phosphoric anhydride when oxygen compounds are employed.

Thus, triphenyl-methane may be obtained (*a*) from benzal chloride and benzene in the presence of aluminium chloride,



$$C_6H_5\cdot CHCl_2 + 2C_6H_6 = CH(C_6H_5)_3 + 2HCl,$$

or from benzaldehyde, benzene, and zinc chloride; (*b*) from chloroform and benzene in presence of aluminium chloride,



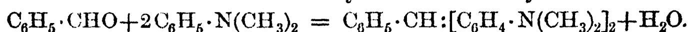
$$3C_6H_6 + CHCl_3 = CH(C_6H_5)_3 + 3HCl;$$

(*c*) from benzhydrol and benzene in the presence of phosphoric anhydride,



$$(C_6H_5)_2CH\cdot OH + C_6H_6 = (C_6H_5)_2CH\cdot(C_6H_5) + H_2O.$$

Derivatives of triphenyl-methane may be obtained by similar methods, *e.g.* the leuco-base of bitter-almond-oil green, tetramethyl-diamino-triphenyl-methane may be prepared by the condensation of benzaldehyde and dimethyl-aniline:

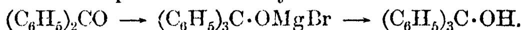


$$C_6H_5 \cdot CHO + 2C_6H_5 \cdot N(CH_3)_2 = C_6H_5 \cdot CH : [C_6H_4 \cdot N(CH_3)_2]_2 + H_2O.$$

When other amines or even phenols are used, a series of allied compounds (which are often dyes) is obtained, the separation of water being facilitated by the addition of zinc chloride, concentrated sulphuric acid, or anhydrous oxalic acid.

Triphenyl-methane, $CH(C_6H_5)_3$ (*Kekulé* and *Franchimont*, B. 5, 906), may be prepared from chloroform and benzene by the *Friedel-Crafts* reaction (cf. A. **194**, 152), diphenyl-methane being produced at the same time; also by eliminating the amino-groups from *p*-leucaniline, $C_{19}H_{13}(NH_2)_3$, and most readily by reducing triphenyl-carbinol with zinc dust and acetic acid. It crystallizes in colourless prisms, m.-pt. 93°, b.-pt. 359°, and dissolves readily in hot alcohol, ether, or benzene.

Like many of its derivatives it crystallises with 1 Mol. C_6H_6. With a carbon disulphide solution of bromine it yields **triphenyl-methyl bromide**, $(C_6H_5)_3 \cdot CBr$, which, when boiled with water, yields **triphenyl-carbinol**, $(C_6H_5)_3C \cdot OH$. This crystallizes in glistening prisms, melts at 159°, and can be sublimed unchanged; it may also be prepared directly by oxidizing a solution of triphenyl-methane in glacial acetic acid with chromic acid, or synthetically by the action of *Grignard's* phenyl magnesium bromide on benzophenone or ethyl benzoate:



$$(C_6H_5)_2CO \longrightarrow (C_6H_5)_3C \cdot OMgBr \longrightarrow (C_6H_5)_3C \cdot OH.$$

A number of homologous and substituted triphenyl-carbinols have been prepared by this last method (*Houben*, B. 1903, 3087), and also by the reaction between an amino-arylketone, sodium and an arylhalide, the sodium first forming a compound of the type $R_2 \cdot CNa \cdot ONa$, which reacts with the arylhalide yielding $R_2 \cdot CR' \cdot ONa$ (*Rodd* and *Linch*, J. A. C. S. 1927, 2174).

Triphenyl-methylamine, $CPh_3 \cdot NH_2$ (B. 1912, **45**, 2910), resembles the carbinol in the readiness with which the NH_2 can be replaced, *e.g.* with ethyl alcohol the NH_2 is replaced by OEt.

Fuming nitric acid converts triphenyl-methane into **trinitro-triphenyl-methane**, $(C_6H_4 \cdot NO_2)_3 \cdot CH$ (yellow scales), which can then be oxidized by chromic acid to **trinitro-triphenyl-carbinol**, $(C_6H_4 \cdot NO_2)_3C \cdot OH$. The latter gives para-rosaniline, $(C_6H_4 \cdot NH_2)_3C \cdot OH$, when reduced with zinc dust and glacial acetic acid.

Homologous with triphenyl-methane are the **tolyl-diphenyl-methanes,** $(C_6H_5)_2CH \cdot C_6H_4 \cdot CH_3$. From these also dyes are derived, especially from *m*-**tolyl-diphenyl-methane** (in which the CH_3 occupies the meta-position with regard to the methane carbon atom), which can be prepared by diazotizing ordinary leucaniline; it crystallizes in small prisms and melts at 59·5°.

TRIPHENYL-METHANE DYES

The entrance of three amino- or hydroxy-groups converts triphenyl-methane and its homologues into the leuco-compounds of dyes, some of which latter are of great value. Two amino-groups suffice for the full development of the dye character only when the amino-hydrogen atoms are replaced by alkyl radicals, one amino-group being insufficient for this (see under *p*-amino-triphenyl-methane).

The following are the chief groups of triphenyl-methane dyes:—

1. Those derived from diamino-triphenyl-methane. The malachite-green group.
2. Those derived from triamino-triphenyl-methane. The rosaniline group.
3. Those derived from trihydroxy-triphenyl-methane. The aurine group.
4. Those derived from triphenyl-methane-carboxylic acid. The eosin group.

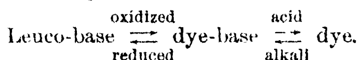
Leuco-bases or **leuco-compounds** of dyes (p. 428) are the colourless compounds formed by the reduction of the dyes, usually by the addition of two atoms of hydrogen. When oxidized they are converted back into the dyes.

All the dyes of the triphenyl-methane group, and also indigo, methylene blue, safranine, &c., are capable of yielding such leuco-compounds, generally on reduction with zinc and hydrochloric acid, stannous chloride, or ammonium sulphide.

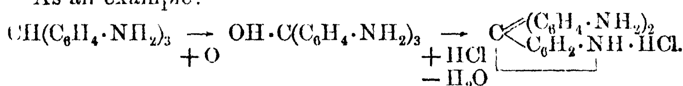
The oxidation of the leuco-compounds is often quickly effected by the oxygen of the air (*e.g.* in the cases of indigo white and of leuco-methylene blue); in the triphenyl-methane group it is slower and frequently more complicated. Leuco-malachite green is readily oxidized to the corresponding colour-base when treated with lead peroxide in acid solution, and leucaniline when warmed with chloranil in alcoholic solution, or when its hydrochloride is heated either alone or

with a concentrated solution of arsenic acid, or with metallic hydroxides such as ferric hydroxide.

The leuco-bases of the triphenyl-methane dyes are derivatives of triphenyl-methane or its homologues, the corresponding dye-bases obtained by oxidizing the leuco-bases are derivatives of triphenyl-carbinol or its homologues, and the dyes themselves are salts obtained by the elimination of water from the dye-base and an acid. The relationships between the three groups of compounds—leuco-base, dye-base, and dyes—are indicated in the following scheme:



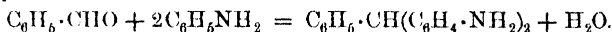
As an example:



1. AMINO- AND DIAMINO- TRIPHENYL-METHANE GROUP

p-**Amino-triphenyl-methane** can be synthesized either by the condensation of *p*-nitro-benzaldehyde with benzene and subsequent reduction, or from benzhydrol and aniline. It forms large prisms, and melts at 84°. The corresponding carbinol is colourless and with acids yields red salts, but these cannot dye animal fibres. (Cf., however, B. 1913, **46**, 70.)

p-**Diamino-triphenyl-methane**, $C_6H_5 \cdot CH(C_6H_4 \cdot NH_2)_2$, is prepared by the action of zinc chloride or of fuming hydrochloric acid upon a mixture of benzaldehyde and aniline sulphate or chloride:



$$C_6H_5 \cdot CHO + 2C_6H_5NH_2 = C_6H_5 \cdot CH(C_6H_4 \cdot NH_2)_2 + H_2O.$$

It crystallizes in prisms, and the colourless salts yield an unstable blue-violet dye, benzal violet, when oxidized. Methylation converts the base into:

Tetramethyl-di-*p*-amino-triphenyl-methane, *leuco-malachite green*, $C_6H_5 \cdot CH[C_6H_4 \cdot N(CH_3)_2]_2$, which is prepared on the technical scale by heating benzaldehyde and dimethyl-aniline with zinc chloride or concentrated sulphuric acid (*O. Fischer*, A. **206**, 103). It forms colourless plates or prisms. As a diacid base it yields colourless salts, which are slowly converted by the air, but immediately by other oxidizing agents, such as lead dioxide and sulphuric acid, into the salts of **tetramethyl-diamino-triphenyl-carbinol**, $C_6H_5 \cdot C(OH)[C_6H_4N(CH_3)_2]_2$.

The free base is obtained by precipitating the salts with alkali. It crystallizes in colourless needles and dissolves in cold acid to a colourless solution; upon warming, however, the intense green coloration of the salts is produced. (See p. 518.)

The double salt with zinc chloride, $(C_{23}H_{25}N_2Cl)_3$, $2\,ZnCl_2$, $2\,H_2O$, or the oxalate, $(C_{23}H_{25}N_2)_2$, $3\,H_2C_2O_4$, of this base is the valuable dye **bitter-almond-oil green**, *malachite green* or *Victoria green*, which forms green plates, readily soluble in water. This can also be prepared directly by heating benzo-trichloride with dimethyl-aniline and zinc chloride (*Doebner*). **Brilliant green** is the tetraethyl compound. The sulphonic acid of the diethyl-dibenzyl-diamino-triphenyl-carbinol is **acid green**.

The fastness of all these dyes is improved by the introduction of an ortho-chlorine atom. Sulphonic acids derived from these chloro-compounds are the **night green**, A., **patent green**, A. G. L., and **brilliant milling green** of commerce.

2. ROSANILINE GROUP

Fuchsine or magenta was first obtained in 1856 by *Natanson*, who noticed the formation of a red substance, in addition to that of aniline hydrochloride and ethylene-aniline, when ethylene chloride was allowed to act upon aniline at a temperature of 200° (A. **93**, 297). It was prepared shortly afterwards by *A. W. Hofmann*, by the action of carbon tetrachloride upon aniline, and was first manufactured on the technical scale in 1859. *Hofmann's* scientific researches on this subject date from 1861. The chemical constitution was made clear by *Emil* and *Otto Fischer* in 1878 (A. **194**, 242). (Cf. also *Caro* and *Græbe*, B. **11**, 1116.)

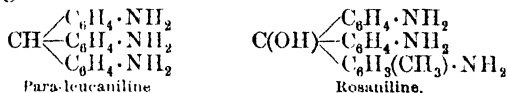
The rosaniline dyes are derived partly from triphenyl-methane and partly from *m*-tolyl-diphenyl-methane; in the former case they are often designated para-compounds (*e.g.* "para-rosaniline", because it is prepared from aniline and para-toluidine; "para-rosolic acid").

Para-leucaniline, *triamino-triphenyl-methane*, $CH(C_6H_4\cdot NH_2)_3$, and **leucaniline,** *triamino-diphenyl-tolyl-methane*, $CH_3\cdot C_6H_3(NH_2)\cdot CH(C_6H_4\cdot NH_2)_2$, are formed by the reduction of the corresponding trinitro-compounds and also of the corresponding dye-bases, para-rosaniline and rosaniline; the first named likewise by the reduction of *p*-nitro-diamino-triphenyl-methane. The free leuco-bases are precipitated by ammonia from solutions of their salts as white or reddish flocculent masses, and crystallize in colourless needles or plates; they melt at 203° and 100° respectively. As bases they form colourless crystalline salts.

Para-rosaniline, $OH \cdot C(C_6H_4NH_2)_3$, and rosaniline, $OH \cdot C \lessgtr \begin{smallmatrix} (C_6H_4 \cdot NH_2)_2 \\ C_6H_3Me \cdot NH_2 \end{smallmatrix}$, are the bases of the fuchsine dyes. They are obtained by precipitating solutions of their salts with alkalis, and crystallize from hot water or alcohol in colourless needles or plates, which become red in the air. Both are tri-acid bases, stronger than ammonia. As they yield tri-diazonium salts on treatment with nitrous acid, they must contain three primary amino-groups. The diazonium compounds readily yield the corresponding hydroxylic dyes, aurine and rosolic acid (p. 522), when boiled with water.

Constitution.—The relations between the rosanilines and tri-phenyl-methane were made clear by *Emil* and *Otto Fischer*, who transformed leucaniline into diphenyl-tolyl-methane by diazotizing and decomposing with alcohol. In a similar manner, para-leucaniline was converted into triphenyl-methane. The two leuco-bases are, therefore, undoubtedly triamino-derivatives of diphenyl-*p*-tolyl-methane and of triphenyl-methane respectively. The dye-bases, which differ from the leuco-bases by one atom of oxygen, are the corresponding carbinol derivatives, *i.e* rosaniline is triamino-diphenyl-*p*-tolyl-carbinol, and para-rosaniline triamino-triphenyl-carbinol.

That the three amino-groups are distributed equally among the three benzene nuclei is clear from the synthesis of para-leucaniline by means of *p*-nitro-benzaldehyde. *p*-Nitro-benzaldehyde, aniline, and sulphuric acid yield *p*-nitro-diamino-triphenyl-methane, $NO_2 \cdot C_6H_4 \cdot CH(C_6H_4 \cdot NH_2)_2$, which, when reduced, yields para-leucaniline. We have, therefore, the following formulæ:



It can be shown that each amino-group occupies the *p*-position with respect to the methane carbon atom. Diamino-triphenyl-methane can be synthesized from benzaldehyde and aniline in the presence of a dehydrating agent. When diazotized and warmed with water, the corresponding dihydroxy-triphenyl-methane is formed, and this, when fused with potash, yields *p*-dihydroxy-benzophenone:



$$C_6H_5 \cdot CH(C_6H_4NH_2)_2 \rightarrow C_6H_5 \cdot CH(C_6H_4 \cdot OH)_2 \rightarrow CO(C_6H_4 \cdot OH)_2$$

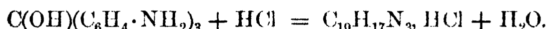
In this last compound the *p*-positions of the hydroxy-groups

have been established, and hence the original amino-groups must also have occupied the *p*-positions, unless intramolecular rearrangement has occurred.

When *p*-nitro-benzaldehyde is condensed with aniline, *p*-nitro-diamino-triphenyl-methane is formed, and the nitro-group must be in the *p*-position, and by analogy with the previous reaction the two amino-groups are also in *p*-positions, and as this compound on reduction yields para-leucaniline it follows that all three amino-groups occupy *p*-positions—a conclusion which is supported by the fact that para-leucaniline can also be transformed into *p*-dihydroxy-benzophenone.

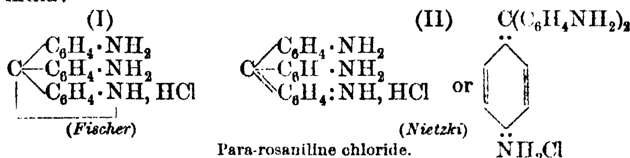
The salts of rosaniline and para-rosaniline, fuchsine, $C_{20}H_{20}N_3Cl$, rosaniline nitrate, $C_{20}H_{20}N_3(NO_3)$, rosaniline acetate, $C_{20}H_{20}N_3(C_2H_3O_2)$, para-fuchsine, $C_{19}H_{18}N_3Cl$, &c., are the actual dyes. While they possess a magnificent fuchsine-red colour in solution, and have intense colouring power (dyeing wool and silk without a mordant), their crystals are of a brilliant metallic green with cantharides lustre, *i.e.* of nearly the complementary colour. They are fairly soluble in hot water and alcohol.

In the formation of the salts, water is eliminated:



$$C(OH)(C_6H_4 \cdot NH_2)_3 + HCl = C_{19}H_{17}N_3, HCl + H_2O.$$

In the dyes there is therefore present a peculiar nitrogen-carbon linking (see formula I), which is reminiscent of the older quinone formula; but the simpler constitution (formula II), which corresponds with the newer quinone formula, is now more generally accepted, and is usually termed the quinonoid formula:



Para-rosaniline chloride.

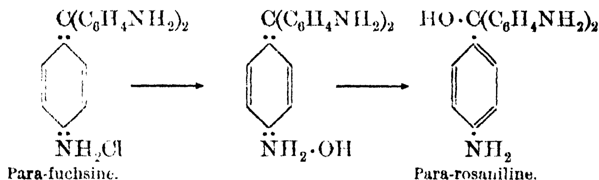
An analogous separation of water is also observed in the formation of salts of the malachite green base, but this only takes place upon warming, as is proved by the fact that it dissolves without colour in cold acids, and that the intense coloration of the salts first becomes apparent after warming the solution.

In addition to the above salts there also exist acid ones, *e.g.* $C_{20}H_{20}N_3Cl + 3HCl$ (which yields a yellow-brown solution,

not a fuchsine-coloured one); these dissociate into the neutral salts and free acid upon the addition of much water. The formation of such acid salts is readily accounted for by the quinonoid formula.

Rosenstiel has suggested the constitution $Cl \cdot C(C_6H_4NH_2)_3$ for para-fuchsine, according to which the salt is the chloride (ester) of a tertiary alcohol. Such a constitution, according to *Hantzsch* and *Osswald* (B. 1900, **33**, 278), is not in harmony with known facts.

Assuming the quinonoid structure II for para-fuchsine, then the conversion into para-rosaniline under the influence of alkalis should be preceded by the formation of an unstable quaternary ammonium hydroxide, which becomes transformed into the carbinol compound, para-rosaniline:

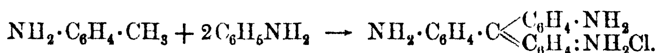


Para-fuchsine. Para-rosaniline.

Hantzsch and *Osswald*, by means of electrical conductivity determinations (B. 1900, **33**, 278), have been able to indicate the presence of such an ammonium derivative in the solution which is formed when the dye is brought into contact with an equivalent of alkali. This compound is coloured in contradistinction to the carbinol base, is very strongly basic and therefore strongly ionized, and is gradually transformed into the insoluble carbinol base. Para-rosaniline and the dye-bases generally are pseudo-bases corresponding in many respects with the pseudo-acids (p. 391).

Formerly in the manufacture of magenta, a mixture of aniline with *o*- and *p*-toluidine was oxidized by syrupy arsenic acid, stannic chloride or mercuric chloride or nitrate, &c.; in the modern method, a mixture of nitro-benzene with aniline and toluidine is heated with iron filings and hydrochloric acid (*Coupier*). Nitro-toluene may also be employed instead of nitro-benzene. If *o*-toluidine is present in the mixture of aniline and *p*-toluidine to be oxidized, rosaniline is formed, and if it is absent, para-rosaniline. When pure aniline is oxidized alone, it yields no fuchsine at all, but products of the nature of indulin. This is explained by the fact that for the

formation of fuchsine a carbon atom is required which shall serve to link the benzene nuclei together, a so-called "methane-carbon"; in the action of carbon tetrachloride upon aniline, this carbon originates from the tetrachloride, and in the oxidation of a mixture of aniline and *p*-toluidine, from the methyl group of the latter, as is shown in the following scheme:



$$NH_2\cdot C_6H_4\cdot CH_3 + 2C_6H_5NH_2 \longrightarrow NH_2\cdot C_6H_4\cdot C\!\left\langle\begin{matrix}C_6H_4\cdot NH_2\\ C_6H_4:NH_2Cl.\end{matrix}\right.$$

Para-rosaniline and rosaniline are also formed by heating *p*-diamino-diphenyl-methane (p. 508) with aniline and *o*-toluidine respectively, in presence of an oxidizing agent (B. **25**, 302).

When rosaniline is heated with hydrochloric or hydriodic acid to 200°, it is split up into aniline and toluidines; when superheated with water, para-rosaniline yields *p*-dihydroxy-benzophenone, ammonia, and phenol. When boiled with hydrochloric acid, rosaniline breaks up into *p*-diamino-benzophenone and *o*-toluidine (B. **16**, 1928; **19**, 107; **22**, 988). A solution of fuchsine is decolorized by sulphurous acid, an additive-product, fuchsine-sulphurous acid, being formed. This solution, *Schiff's* reagent, is a delicate reagent for aldehydes, which colour it violet-red (see p. 127; B. **21**, Ref. 149, &c.).

Formaldehyde and *o*-toluidine yield methylene *o*-toluidine, $CH_2:N\cdot C_6H_4\cdot CH_3$, which consenses with *o*-toluidine and its hydrochloride, yielding diamino-*o*-tritolylmethane, which can be oxidized to the dye **new magenta.**

1. **Methylated rosanilines** (*Hofmann, Lauth*).—The red colour of para-rosaniline and of rosaniline is changed into violet by the entrance of methyl or ethyl groups, the intensity of the latter colour increasing with an increasing number of these groups. The salts of **hexamethyl-para-rosaniline** have a magnificent bluish-violet shade. In the manufacture of these "methyl-violets" one may either (1) methylate rosaniline (by means of CH_3Cl or CH_3I); or (2) oxidize, instead of aniline, a methylated aniline such as dimethyl-aniline by means of cupric salts, whereby para-rosaniline derivatives result; or (3) allow phosgene to act upon dimethyl-aniline (or the latter to act upon the tetramethyl-diamino-benzophenone first produced):

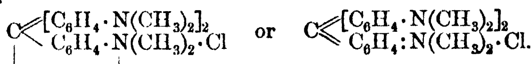


$$COCl_2 + 3C_6H_5\cdot N(CH_3)_2 = C(OH)[C_6H_4\cdot N(CH_3)_2]_3 + 2HCl.$$

In the last case hexamethyl-violet, termed "**crystal violet**" on account of the beauty of its crystals, is formed, while the

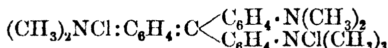
methyl-violets prepared by methods (1) and (2) are mixtures of hexa-, penta-, and tetramethyl-rosanilines and are amorphous.

The hydrochloride of the hexamethyl dye has the constitution:



An interesting synthesis of this compound is by the action of the magnesium derivative of *p*-bromo-dimethyl-aniline on tetramethyl-diamino-benzophenone and subsequent treatment with hydrochloric acid (cf. Synthesis of Tertiary Alcohols, p. 126).

The hexamethyl-carbinol no longer contains an amino-hydrogen atom, in consequence of which any further methyl chloride or iodide cannot effect an exchange of hydrogen for alkyl, but can only form an additive compound, a quaternary ammonium salt. Such addition causes a change of colour from violet to green; thus the compound



is the dye **methyl green** or *light green*. **Ethyl green** (ethyl-hexamethyl rosaniline) is formed by the action of ethyl bromide on methyl violet.

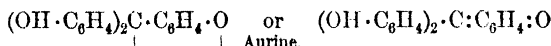
Various **ethyl violets** are known corresponding with the methyl violets. The hexa-substituted rosanilines, which contain benzyl as well as methyl or ethyl groups, are similar to crystal violet; their sulphonic acids form useful dyes, *e.g.* acid **violet**.

2. **Phenylated rosanilines**. By the successive entrance of phenyl-groups into rosaniline, there are formed in the first instance violet dyes, which change to blue when three phenyl groups have entered. **Triphenyl-fuchsine** or "**aniline blue**" is a beautiful blue dye, insoluble in water but soluble in alcohol. It is prepared by heating rosaniline with aniline in presence of benzoic acid, when ammonia is eliminated; or by the oxidation of phenylated aniline, *i.e.* diphenylamine, *e.g.* by means of oxalic acid. The latter supplies the "methane carbon atom", and the beautiful "diphenylamine blue" or **spirit blue** which is formed is a para-rosaniline derivative. Formic aldehyde can also supply the methane carbon atom.

Dyes insoluble in water are converted into soluble sulphonic **acids**. Such acids are **Nicholson's blue, water blue,** and **light blue**. **Patent blue, new patent blue,** are disulphonic acids.

3. TRIHYDROXY-TRIPHENYL-METHANE, $CH(C_6H_4 \cdot OH)_3$, OR THE AURINE GROUP

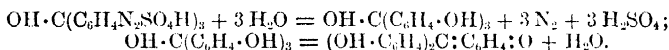
The hydroxy-analogues of para-rosaniline and rosaniline are **aurine**, $C_{19}H_{14}O_3$, and **rosolic acid**, $C_{20}H_{16}O_3$:



$$(OH \cdot C_6H_4)_2C \cdot C_6H_4 \cdot O \quad \text{or} \quad (OH \cdot C_6H_4)_2 \cdot C{:}C_6H_4{:}O$$

Aurine.

These likewise possess the dye character, but, instead of being basic, they are acid dyes (phenol dyes); they are of far less value than the basic dyes which have been already described. They are formed when the diazonium derivatives of para-rosaniline or rosaniline are boiled with water (*Caro* and *Wanklyn*, 1866):



$$OH \cdot C(C_6H_4N_2SO_4H)_3 + 3\,H_2O = OH \cdot C(C_6H_4 \cdot OH)_3 + 3\,N_2 + 3\,H_2SO_4;$$
$$OH \cdot C(C_6H_4 \cdot OH)_3 = (OH \cdot C_6H_4)_2C{:}C_6H_4{:}O + H_2O.$$

The carbinol which must be produced here in the first instance is incapable of existence, and loses water. The constitutional formulæ follow from this close relation to the rosanilines.

Aurine is also obtained by heating phenol with oxalic and sulphuric acids to 130°–150° (*Kolbe* and *Schmitt*, 1859), the oxalic acid yielding the "methane carbon atom"; rosolic acid results in an analogous manner from a mixture of phenol and cresol with arsenic and sulphuric acids. Phenol by itself yields no rosolic acid upon oxidation.

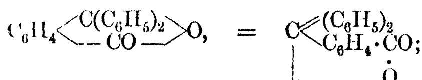
Aurine and rosolic acid crystallize in beautiful green needles or prisms with a metallic lustre, dissolve in alkalis with a fuchsine-red colour, and are thrown down again from this solution by acids. The alkaline salts are decidedly unstable, aurine being but a weak phenol; at the same time it possesses a slightly basic character. An ammonium salt is known which crystallizes in dark-red needles with a blue lustre. Upon reduction there are formed the leuco-compounds **leucaurine**, $CH(C_6H_4 \cdot OH)_3$, and **leuco-rosolic acid**, $OH \cdot C_6H_3Me \cdot CH(C_6H_4 \cdot OH)_2$, both of which crystallize in colourless needles of phenolic character. Superheating with water transforms aurine into *p*-dihydroxy-benzophenone, $CO(C_6H_4 \cdot OH)_2$, and phenol; superheating with ammonia, into para-rosaniline.

Chrome violet, prepared from formaldehyde, salicylic acid, and sulphuric acid, is sodium-aurine-tricarboxylate.

4. TRIPHENYL-METHANE-CARBOXYLIC ACID, OR THE EOSIN GROUP

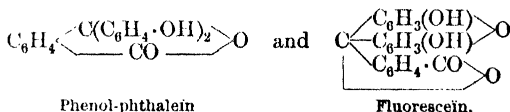
Triphenyl-methane-carboxylic acid, $CH(C_6H_5)_2(C_6H_4 \cdot CO_2H)$, obtained by the reduction of phthalophenone (see below), crystallizes in colourless needles melting at 162° and yields triphenyl-methane by the elimination of carbon dioxide.

Triphenyl-carbinol-*o*-carboxylic acid, $OH \cdot C(C_6H_5)_2(C_6H_4 \cdot CO_2H)$. The anhydride of this acid, which is termed **phthalophenone**, is obtained by heating phthalyl chloride with benzene and aluminium chloride (A. **202**, 50), and forms plates, melting at 115°. The acid itself is incapable of existence, but its salts are obtained by dissolving the anhydride in alkalis. Phthalophenone is on the one hand a triphenyl-methane derivative and on the other a derivative of phthalic acid; in accordance with the constitutional formula:



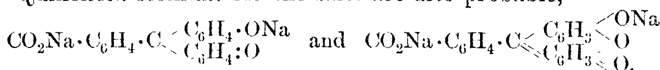
it is to be regarded as diphenyl-phthalide (Phthalide, p. 493).

Phthalophenone is the mother substance of a large series of dyes, which are derived from it by the entrance either of hydroxyl or of amino-groups. They are prepared by the action of phenols upon phthalic anhydride, and are termed *Phthaleins.* Phenol and resorcinol, for example, yield the compounds:



Phenol-phthaleïn Fluoresceïn.

Quinonoid formulæ for the salts are also probable,

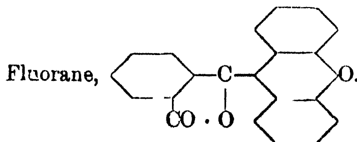


Free phenol-phthaleïn, which is colourless, probably has the lactone formula, and its coloured salts the quinonoid structure. Phenol-phthaleïn would then be a *pseudo-acid* (p. 392). A large excess of alkali transforms the coloured salts into colourless ones, probably $CO_2Na \cdot C_6H_4 \cdot C(OH)(C_6H_4 \cdot ONa)_2$. See *H. Meyer*, M. 1899, **20**, 337; B. **36**, 2949; **38**, 1318; *Green* and others, J. C. S. 1904, 398; B. **39**, 2365; **40**, 3724; *Stieglitz*, J. A. C. S. **25**, 1112; *Acree*, Am. C. J. **39**, 528, 771; **42**, 115; *Kehrmann*, A. **372**, 287; B. **45**, 3346, 3504; *Liebig*, J. pr. **85**, 97, 241.

In the case of fluoresceïn a molecule of water is split off from two hydroxyls of the two resorcinol residues. Phthaleïns of this kind (being hydroxy-phthalophenones) are converted by reduction into the hydroxy-derivatives of triphenyl-methane-carboxylic acid, which are termed "*Phthalines*"; *e.g.* phenol-phthaleïn into dihydroxy-triphenyl-methane-carboxylic acid (*i.e.* phenol-phthaline), $CH{<}^{(C_6H_4 \cdot OH)_2}_{C_6H_4 \cdot CO_2H}$. The phthalines are colourless, and are to be looked upon as leuco-compounds of the phthaleïns. The phthaleïns include many dyes which are of technical value, *e.g.* the eosins (*Caro*, *Baeyer*, 1871).

Phenol-phthaleïn is prepared by heating phthalic anhydride with phenol and sulphuric acid, or better, stannic chloride (or oxalic acid), to 115°–120°. It may also be obtained by nitrating diphenyl-phthalide, reducing the two substituting nitro-groups, and replacing the amino-groups thus formed by hydroxyl in the usual manner (A. **202**, 68). It crystallizes from alcohol in colourless crusts; is nearly insoluble in water, but dissolves in dilute alkalis with a beautiful red colour which vanishes again on neutralization with acids; it is thus a valuable indicator. With very concentrated alkalis phenol-phthaleïn yields colourless solutions (cf. p. 523). A colourless and a red ethyl derivative are known corresponding with the lactone and quinone structures. The *p*-positions of the two hydroxy-groups have been proved by conversion into *p*-dihydroxy-benzophenone. It yields a **di-acetyl** derivative melting at 143° and an **oxime** melting at 212°. It is reduced by potash and zinc dust to **phenol-phthaline** (colourless needles), which dissolves in alkali to a colourless solution, but is readily reoxidized in this solution to phenol-phthaleïn. When treated with magnesium methyl iodide it does not show the presence of active hydrogen atoms, whereas fluoresceïn contains two active hydrogen atoms (G. 1912, **42**, ii, 204).

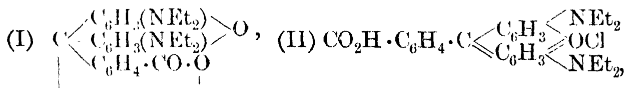
Fluorane, $C_{20}H_{12}O_3$, is formed as a by-product in the phenol-phthaleïn melt, and is the mother substance of fluoresceïn, and like pyrone can give rise to oxonium salts. The whole group of dyes is often known as the **Pyronine** group.

Fluorane, 

Fluoresceïn, *Dihydroxy-fluorane* or *resorcinol-phthaleïn*, $C_{20}H_{12}O_5 + H_2O$, is prepared by heating phthalic anhydride and resorcinol at 200°. It forms a dark-red crystalline powder, and dissolves in alcohol with a yellow-red colour, and in alkalis with a red colour and splendid green fluorescence. It is reducible to the phthaline "Fluorescin", and with bromine yields red crystals of tetrabromo-fluoresceïn, the potassium salt of which, $C_{20}H_6Br_4O_5K_2$, is the magnificent dye **eosin.** Fluorescing dyes are likewise formed in an analogous manner from all the derivatives of 1:3-dihydroxy-benzene, in which position 5 is unoccupied, and the reaction is often made use of on the one hand for testing for *m*-dihydroxy-derivatives, and on the other for phthalic anhydride or succinic anhydride.

Instead of phthalic acid itself, chlorinated or brominated, &c., phthalic acids may be employed, so that, by gradually increasing the amount of halogen present, a whole series of yellow-red to violet-red eosins can be prepared, *e.g.* tetrabromo-di-iodo-eosin; these are known under the names of Erythrosin, Rose de Bengale, Phloxin, &c. It is worthy of note that many other dibasic acids (*e.g.* succinic) and also benzoic acid are capable of yielding fluorescing compounds. **Gallein,** $C_{20}H_{12}O_7$, is the dye obtained from pyrogallol and phthalic anhydride.

The **rhodamines** are dyes closely allied to fluoresceïn. They are obtained by the condensation of phthalic anhydride and *p*-alkylated-amino-phenols in presence of sulphuric acid. They contain the pyrone ring, and may be regarded as fluoresceïn in which the two hydroxyl groups have been replaced by tertiary amino-groups. **Tetra-ethyl rhodamine** (I),



is colourless, and has basic properties. The salts, *e.g.* chloride, **Rhodamine B**, are red dyes, and probably possess either a quinonoid or oxonium (II) structure.

Tetraphenyl-methane, $C(C_6H_5)_4$.—Triphenyl-bromo-methane and phenyl-hydrazine yield $CPh_3 \cdot NH \cdot NHPh$, triphenylmethane-hydrazobenzene, which gives the corresponding azo-compound when oxidized, $CPh_3 \cdot N:NPh$, and when this is heated nitrogen is evolved and tetraphenyl-methane is formed.

It is more readily prepared by the action of magnesium phenyl bromide on triphenyl-chloro-methane (B. 1906, **39**, 1462), and forms colourless crystals, melting at 282°.

s-**Tetraphenylethane**, $CHPh_2 \cdot CHPh_2$, is readily synthesized by the action of benzenediazonium sulphate on copper acetylide, $4\,N \vdots NPhSO_4H + 2\,CuC \vdots CCu \longrightarrow CHPh_2 \cdot CHPh_2 + 4\,CuSO_4$; diphenyl is formed as a by-product. (J. russ. 1916, **48**, 253.)

XXXI. COMPOUNDS WITH CONDENSED BENZENE NUCLEI. NAPHTHALENE GROUP

The higher fractions of coal-tar contain hydrocarbons of high molecular weight, especially naphthalene, $C_{10}H_8$, anthracene, $C_{14}H_{10}$, and its isomeride phenanthrene. The first-named is found in the fraction between 180°–200°, and the two latter in that between 340°–360°.

These compounds are of more complex composition than benzene, the molecule of naphthalene differing from that of the latter by C_4H_2, and those of anthracene and phenanthrene from that of naphthalene by the same increment. They closely resemble benzene as regards behaviour, and give rise to types of derivatives similar to those of benzene itself.

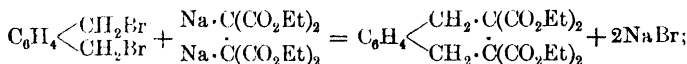
They undoubtedly contain benzene nuclei, as anthracene yields benzoic acid upon oxidation, naphthalene phthalic acid, and phenanthrene diphenic acid.

NAPHTHALENE GROUP

Naphthalene, $C_{10}H_8$, discovered by *Garden* in 1820, is contained in coal-tar and crystallizes from the fraction boiling at 180°–200°. The crystals are pressed to remove oily impurities, and are further purified by treatment with small amounts of concentrated sulphuric acid and subsequent sublimation.

It is also formed when various carbon compounds are subjected to a red heat; thus, together with benzene, styrene, &c., by passing the vapours of methane, ethylene, acetylene, alcohol, acetic acid, &c., through red-hot tubes. Naphthalene derivatives are formed when many sesquiterpenes (chap. XLI) are heated with sulphur. The constitutional formula (p. 528) is largely based on the following syntheses:—

1. By the action of *o*-xylylene bromide upon the sodium compound of the symmetrical ethane-tetracarboxylic ester, ethyl tetrahydronaphthalene-tetracarboxylate is formed:

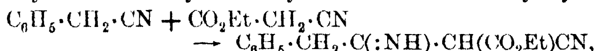


$$C_6H_4<\begin{matrix}CH_2Br\\CH_2Br\end{matrix} + \begin{matrix}Na\cdot C(CO_2Et)_2\\ Na\cdot C(CO_2Et)_2\end{matrix} = C_6H_4<\begin{matrix}CH_2\cdot C(CO_2Et)_2\\ CH_2\cdot C(CO_2Et)_2\end{matrix} + 2NaBr;$$

and from this, naphthalene may be obtained by hydrolysis, the elimination of the carboxyl groups and subsequent oxidation (*Baeyer* and *Perkin*, B. **17**, 448).

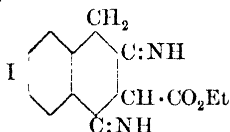
2. α-Naphthol, $C_{10}H_7\cdot OH$, is produced by the elimination of water from γ-phenyl-isocrotonic acid (*Fittig* and *Erdmann*, B. **16**, 43; see p. 486), and yields naphthalene when heated with zinc dust.

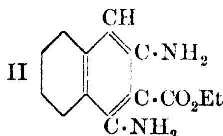
3. *J. F. Thorpe* (P. 1905, **21**, 305) has succeeded in synthesising a number of naphthalene derivatives by means of ethyl sodio-cyano-acetate, *e.g.* ethyl 1:3-diamino-naphthalene-2-carboxylate from ethyl sodio-cyano-acetate and benzyl cyanide.



$$C_6H_5\cdot CH_2\cdot CN + CO_2Et\cdot CH_2\cdot CN \longrightarrow C_6H_5\cdot CH_2\cdot C(:NH)\cdot CH(CO_2Et)CN,$$

and this with sulphuric acid yields the bicyclic compound I, which is immediately transformed into the diamino-derivative II.



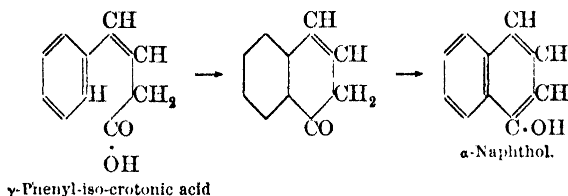


The same compound may be synthesised from ethyl sodio-cyano-acetate by the following stages (J. C. S. 1907, **91**, 578). Condensed with *o*-toluyl chloride, $CH_3\cdot C_6H_4\cdot CO\cdot Cl$, it yields ethyl cyano-*o*-toluyl-acetate, $CH_3\cdot C_6H_4\cdot CO\cdot CH(CN)CO_2Et$, and this when heated with ammonium acetate gives the corresponding imino-derivative, $CH_3\cdot C_6H_4\cdot C(:NH)\cdot CH(CN)CO_2Et$, ethyl β-imino-α-cyano-β-*o*-tolyl-propionate, which reacts with acids giving compound I.

1:4-Naphthalene-diamines have been prepared by similar methods, using derivatives of phenyl-butyric acid (J. C. S. 1907, **91**, 1004).

Constitution.—That naphthalene contains a benzene nucleus, in which two hydrogen atoms occupying the ortho-position are replaced by the group $(C_4H_4)''$, follows not only from its oxidation to phthalic acid, but also from its formation from

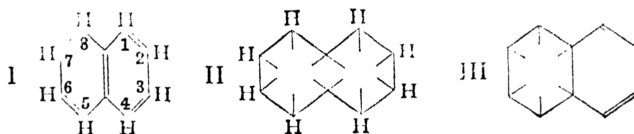
o-xylylene bromide. And that the four carbon atoms of this group are linked to one another without branching is shown by the formation of α-naphthol.



That there are actually two so-called "condensed" benzene nuclei present in the naphthalene molecule is a conclusion drawn from experiments of the following type:—

α-Nitro-naphthalene (p. 531) on oxidation yields nitrophthalic acid, $C_6H_3(NO_2)(CO_2H)_2$; consequently the benzene ring to which the nitro-group is linked remains intact. But, on reducing the nitro-naphthalene to amino-naphthalene and oxidizing the latter, no amino-phthalic acid nor any oxidation product of it is obtained, but phthalic acid itself, a proof that this time the benzene nucleus to which the amino-group is attached has been destroyed, and that the other has remained intact (*Graebe*, 1880; for an analogous proof by him, see A. **149**, 20).

Naphthalene therefore receives the constitutional formula I (*Erlenmeyer*, 1866)



There is the same difficulty in deciding between the double bond *Kekulé* formula and the centric formula II (*Bamberger*) as in the case of benzene; and probably formula III, suggested by *Harries* (A. 1905, **343**, 311), is most in harmony with the behaviour of napthalene on oxidation and reduction. (Cf., however, *Stark*, Abs. 1913, ii, 366.)

The above constitutional formula is in complete harmony with the number of isomeric forms in which naphthalene derivatives occur, and also with the formation of additive compounds with hydrogen or chlorine.

This union of two benzene nuclei is accompanied by a modification of their properties, so that naphthalene and its derivatives differ characteristically from benzene in many respects. Such differences show themselves, for instance, between the naphthylamines and aniline, the naphthols and phenol; and also especially in the greater readiness with which the naphthalene derivatives are reduced, the latter taking up as many as four atoms of hydrogen easily.

After such addition the reduced nucleus is found to have entirely lost the characteristics of a benzene nucleus, and to have become similar in properties to an alphyl radical, whereas the non-reduced nucleus assumes the character of a benzene nucleus in its entirety (*Bamberger*). (See the Tetrahydro-derivatives of the Naphthylamines and Naphthols, pp. 532 and 534.)

Properties.—Naphthalene crystallizes in glistening plates, is insoluble in water, sparingly soluble in cold alcohol and ligroïn, but dissolves readily in hot alcohol and ether; it melts at 80° and boils at 218°. It has a characteristic tarry smell, and is distinguished by the ease with which it sublimes and volatilizes with steam.

With picric acid it yields an additive compound, $C_{10}H_8$, $OH \cdot C_6H_2(NO_2)_3$, crystallizing in yellow needles and melting at 149°. It takes up hydrogen far more readily than benzene does, yielding di- and **tetrahydronaphthalenes**, $C_{10}H_{10}$ and $C_{10}H_{12}$; both of these are liquids of pungent odour which regenerate naphthalene again when heated. By catalytic hydrogenation, the second benzene nucleus can also be made to take up hydrogen, a **dekahydronaphthalene**, $C_{10}H_{18}$, is formed, for stereochemistry of dekahydronaphthalene and its derivatives see chap. XLVI, A. It also yields additive products with chlorine more readily than benzene does, *e.g.* **naphthalene dichloride**, $C_{10}H_8Cl_2$, and **-tetrachloride**, $C_{10}H_8Cl_4$ (m.-pt. 182°); the latter is oxidized to phthalic acid more easily than naphthalene itself, hence that acid is sometimes prepared from it on the large scale.

Naphthalene is principally used for the preparation of phthalic acid (for eosin, indigo, &c.), and of naphthylamines and naphthols (for azo-dyes); also for the carburation of illuminating gas. It is a powerful antiseptic, and is used therapeutically.

NAPHTHALENE DERIVATIVES

The number of substitution products in the case of naphthalene is greater than with benzene.

The mono-derivatives invariably exist in two isomeric forms, the α- and β-compounds, e.g.:

$C_{10}H_7Cl$ (α- and β-chloro-naphthalene).
$C_{10}H_7NH_2$ (α- and β-naphthylamine).
$C_{10}H_7OH$ (α- and β-naphthol).
$C_{10}H_7CH_3$ (α- and β-methyl-naphthalene).

As in the case of the benzene compounds, the existence of two series of mono-derivatives has not only been established empirically, but it has also been proved (in a manner similar to that given on p. 354, *et seq.*) that in the naphthalene molecule two sets of hydrogen atoms (the α and β, α = 1, 4, 5, 8; β = 2, 3, 6, 7) have an equal value as regards one another, but the atoms of the one set differ from those of the other, so that the α- and the β-positions occur severally four times, *i.e.* twice in each benzene nucleus (*Atterberg*).

The above constitutional formula for naphthalene satisfies these conditions, since, according to it, the positions 1, 4, 5, and 8 are severally equal and also the positions 2, 3, 6, and 7, but not the positions 1 and 2. The conception that in the α-compounds the position 1, 4, 5, or 8 is occupied is due to *Liebermann* (A. 183, 225), *Reverdin* and *Noelting* (B. 13, 36), and *Fittig* and *Erdmann* (cf. the formation of α-naphthol given above).

With regard to the di-derivatives of naphthalene, a considerable number of isomerides of a good many are known; according to the naphthalene formula, ten are theoretically possible in each case when the two substituents are the same, and fourteen when they are different. The ten possible isomerides are 1:2, 1:3, 1:4, 1:5, 1:6, 1:7, 1:8, 2:3, 2:6, and 2:7. All other combinations are identical with one of these ten. According to *Armstrong* and *Wynne* ten dichloro- and fourteen trichloro-naphthalenes are actually known. (See also B. 1900, 33, 1910, 2131.)

The position 1:8 is termed the "*peri-*" position; it resembles the ortho- position to some extent, *e.g. peri*-naphthalene-dicarboxylic acid like an *o*-dicarboxylic acid yields an anhydride.

The **homologues** of naphthalene are of comparatively small importance, and are usually prepared by *Fittig's* or by *Friedel* and *Crafts'* synthesis. Most of them are liquids, and on oxidation yield acids resembling benzoic acid.

α-Bromo-naphthalene can be prepared directly by brominating naphthalene, and is partially converted into the β-compound

when heated with aluminium chloride. Its bromine atom is somewhat more readily exchangeable than that of bromobenzene, but cannot be eliminated by boiling with alkalis. Interesting methods of formation of the halogen derivatives are by heating the hydroxy-, nitro-, or sulphonic acid derivatives with phosphorus pentachloride.

α-**Nitro-naphthalene**, $C_{10}H_7 \cdot NO_2$ (*Laurent*, 1835), is formed by the direct nitration of naphthalene. It crystallizes in yellow prisms, melts at 61°, boils without decomposition, and readily yields 1:5 and 1:8 di- and various tri- and tetra-nitronaphthalenes upon further nitration. On reduction it is converted into α-naphthylamine. The position of the nitro-group has been established by conversion of this compound into α-naphthol.

The isomeric β-**nitro-naphthalene** can be obtained indirectly by diazotizing β-naphthylamine, and acting on the product with sodium nitrite in presence of cuprous oxide (B. **20**, 1494; **36**, 4157); it crystallizes in bright yellow needles melting at 79°.

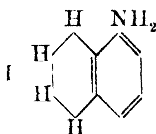
α-**Naphthylamine**, $C_{10}H_7 \cdot NH_2$ (*Zinin*), forms colourless needles or prisms, melts at 50°, boils at 300°, and is readily soluble in alcohol. It can be obtained by reducing the α-nitro-compound, and also readily by heating α-naphthol with the double compound of calcium chloride and ammonia, while aniline can only be prepared from phenol in a similar manner with difficulty: $C_{10}H_7 \cdot OH + NH_3 = C_{10}H_7 \cdot NH_2 + H_2O$.

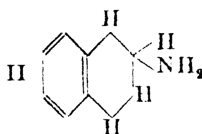
It possesses a disagreeable fæcal-like odour, sublimes readily, and turns brown in the air. Certain oxidizing agents, such as ferric chloride, produce a blue precipitate with solutions of its salts, while others give rise to a red oxidation product; chromic anhydride oxidizes it to α-naphthaquinone. In other respects it resembles aniline; for differences, see B. **23**, 1124. Its hydrochloride is only sparingly soluble in water.

The isomeric β-**naphthylamine**, $C_{10}H_7 \cdot NH_2$ (*Liebermann*, 1876), is most conveniently prepared by heating β-naphthol either in a stream of ammonia or with the double compound of zinc chloride and ammonia. It is now generally prepared by the action of ammonium hydroxide and sulphite on β-naphthol (C. C. 1901, **1**, 349). Naphthyl ammonium sulphite is formed as an intermediate product and reacts with the ammonia, yielding naphthylamine and ammonium sulphite. This reaction is frequently used for transforming derivatives of α and β naphthol into corresponding amino-compounds. The reaction is reversible and can be used for replacing NH_2 by OH.

β-Naphthylamine crystallizes in nacreous plates, melts at 112°, boils at 294°, and has no odour. It is more stable than α-naphthylamine, and is not coloured by oxidizing agents.

Both of these naphthylamines can be converted into tetrahydro-compounds by the action of sodium and amyl alcohol (*i.e.* nascent hydrogen) upon them. The **tetrahydro-α-naphthylamine** resembles its mother substance closely in most of its properties, *e.g.* it can be diazotized and has entirely assumed the character of aniline; the hydrogen atoms have entered the nucleus which does not contain the amino-group. It is termed *aromatic* or "*ar*"-tetrahydro-α-naphthylamine. (Formula I.) **Tetrahydro-β-naphthylamine**, on the other hand, is not diazotized by nitrous acid, but transformed into a very stable nitrite. Here it is the benzene nucleus containing the amino-group which has become reduced; the compound has assumed the properties of an amine of the fatty series, and is termed *alicyclic* or "*ac*"-tetrahydro-β-naphthylamine. (Formula II.) The α-compound is oxidizable to adipic acid (p. 239), and the β-compound to *o*-hydrocinnamo-carboxylic acid, $C_6H_4<^{CH_2 \cdot CH_2 \cdot CO_2H}_{CO_2H}$. (Cf. *Bamberger* and others, B **21**, 847, 1112, 1892; **22**, 625, 767; **23**, 876, 1124.)

I 

II 

An ac-tetrahydro-α- and an **ar-tetrahydro-β-naphthylamine** have also been prepared.

From both naphthylamines there are derived, as in the benzene series, **methyl- and dimethyl-naphthylamines, phenyl-α- and -β-naphthylamines** (which are of technical importance), **nitro-naphthylamines**, diamino-naphthalenes or **naphthylene-diamines**, $C_{10}H_6(NH_2)_2$, **diazonium-compounds** (which are in every respect analogous to the diazonium salts of benzene, especially in the formation of azo-dyes, many of which are of great technical importance), **diazo-amino-compounds**, &c.

The **diazo-amino-naphthalene**, $C_{10}H_7 \cdot N : N \cdot NH \cdot C_{10}H_7$, which is formed by the action of nitrous acid upon α-naphthylamine, readily undergoes a molecular transformation (like the corresponding benzene compound) into **amino-azo-naphthalene**,

$C_{10}H_7 \cdot N:N \cdot C_{10}H_6 \cdot NH_2$. This latter compound crystallizes in brownish-red needles with a green metallic lustre, and can be diazotized, its diazo-compound yielding **α-azo-naphthalene**, $C_{10}H_7 \cdot N:N \cdot C_{10}H_7$ (red to steel-blue glistening prisms), when boiled with alcohol. This last is not readily obtained by the methods which hold good for azo-benzene.

A mixture of **naphthalene** α- and **β-sulphonic acids**, $C_{10}H_7 \cdot SO_2 \cdot OH$, is obtained by warming naphthalene to 80° with concentrated sulphuric acid. They may be separated by aid of their calcium or barium salts, as the β-sulphonates are less soluble than the α-salts. The α-acid is transformed into the β-acid when heated with concentrated sulphuric acid, and hence the chief product obtained by sulphonating naphthalene at 160° is the β-acid (*Witt*, B. 1915, **48**, 743). The sulphonic acid radicals in these compounds may be more readily replaced by hydroxyl or cyanogen than in the benzene series (B. 1914, **47**, 3160).

Naphthalene-disulphonic acids, $C_{10}H_6(SO_3H)_2$.—Two isomeric β-β-acids (2:6 and 2:7) are formed when naphthalene is heated with concentrated sulphuric acid at 160°–200°, while an α-α-acid (1:5) is obtained with chloro-sulphonic acid, SO_3HCl, in the cold, and the α-β-acid (1:6) from the β-mono-sulphonic acid in a similar manner.

Naphthylamine-mono-sulphonic acids, $NH_2 \cdot C_{10}H_6 \cdot SO_2 \cdot OH$.—Thirteen isomers of these are known (7 α- and 6 β-). **Napthionic acid** ($NH_2 : SO_3H = 1:4$) is obtained by the sulphonation of α-naphthylamine; it is employed in the preparation of azo-dyes, as are also several of its isomers and various **naphthylamine-disulphonic acids**. These last are obtained (*a*) directly from α- or β-naphthylamine (*Green* and *Vakil*, J. C. S. 1918, **113**, 35), or (*b*) by nitrating the naphthalene-sulphonic acids and then reducing to the amine.

α- and β-**Naphthols**, $C_{10}H_7 \cdot OH$, which are present in coal-tar, can be easily prepared, not only from the naphthalene-sulphonic acids as above, but also by diazotizing the naphthylamines. They crystallize in glistening plates, have a phenolic odour, and dissolve readily in alcohol and ether but only sparingly in hot water. α-Naphthol (*Griess*, 1866) melts at 95° and boils at 282°, while β-naphthol (*Schäffer*, 1869) melts at 122° and boils at 288°; both of them are readily volatile at ordinary temperatures. They possess a phenolic character, but nevertheless resemble the alcohols of the benzene series more than the phenols, their hydroxy-groups being much more reactive

Carboxylic Acids.—The **naphthoic acids**, $C_{10}H_7 \cdot CO_2H$, can be obtained by saponifying the cyano-naphthalenes and also by the other synthetical methods given for the acids of the benzoic series. They crystallize in fine needles sparingly soluble in hot water, and break up into naphthalene and carbon dioxide when distilled with lime. From them are derived the **hydroxy-naphthoic acids**, $C_{10}H_6(OH)(CO_2H)$, which are related to salicylic acid or its isomers. Among the **naphthalene-dicarboxylic acids**, $C_{10}H_6(CO_2H)_2$, which are known may be mentioned **naphthalic acid**, (1 : 8), which at a somewhat high temperature yields an anhydride similar to phthalic anhydride.

Phenyl-naphthalene, $C_{10}H_7(C_6H_5)$, has also been prepared; it is a compound built up of a naphthalene and of a benzene nucleus, and is therefore analogous to diphenyl, $C_6H_5 \cdot C_6H_5$. The same applies to:

Di-naphthyl, $C_{10}H_7 \cdot C_{10}H_7$, which yields derivatives (*e.g.* the di-naphthols, see p. 534) analogous to those of diphenyl. The three modifications which are theoretically possible, namely the *α*-*α*-, *β*-*β*-, and *α*-*β*-compounds, are known.

Another derivative of naphthalene is **acenaphthene**, $C_{12}H_{10}$, $= C_{10}H_6 \left\langle \begin{matrix} CH_2 \\ CH_2 \end{matrix} \right\rangle$ (1 : 8), which is found in coal-tar. It crystallizes in colourless prisms, melts at 95°, boils at 277°, and yields naphthalic acid on oxidation. When passed through a red-hot tube it yields **acenaphtylene**, $C_{10}H_{16} \left\langle \begin{matrix} CH \\ CH \end{matrix} \right\rangle$, yellow crystals, m.-p. 93°.

XXXII. THE ANTHRACENE AND PHENANTHRENE GROUPS

A. Anthracene

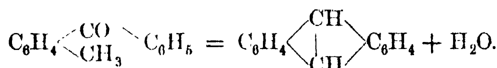
Anthracene, $C_{14}H_{10}$ (*Dumas* and *Laurent*, 1832; *Fritzsche*, 1857), is formed, together with benzene and naphthalene, by the destructive distillation of coal and, generally, by the pyrogenous reactions which give rise to these products, *e.g.* by passing CH_4, C_2H_6, C_2H_2, the vapour of alcohol, &c., through red-hot tubes.

Although coal-tar contains only some 0·25–0·45 per cent of anthracene, it is the chief source from which this hydrocarbon

is obtained. The fraction of coal-tar distilling above 270° and known as anthracene oil yields, on further distillation and ligesting with solvent naphtha, a solid mass known as 50-per-cent anthracene, which is then distilled with one-third of of its weight of potassium carbonate. This serves to remove carbazole (p. 505), which yields a non-volatile potassium derivative $\begin{matrix} C_6H_4 \\ \cdot \\ C_6H_4 \end{matrix}\!\!>\!NK$, and the distillate consists of anthracene and phenanthrene. The phenanthrene is removed by extraction with carbon disulphide, and the anthracene crystallized from benzene.

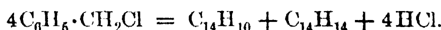
The following are some of the more important methods by means of which the hydrocarbon has been synthesised, and they throw considerable light upon its constitution:—

1. By heating *o*-tolyl phenyl ketone with zinc dust (B. **7**, 17):



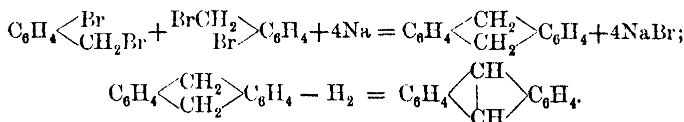
$$C_6H_4<^{CO}_{CH_3}>C_6H_5 = C_6H_4<^{CH}_{CH}>C_6H_4 + H_2O.$$

2. Together with dibenzyl, by heating benzyl chloride with water at 200° (B. **7**, 276):



$$4C_6H_5\cdot CH_2Cl = C_{14}H_{10} + C_{14}H_{14} + 4HCl.$$

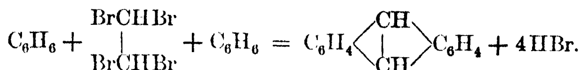
3. From *o*-bromo-benzyl bromide and sodium in ethereal solution dihydro-anthracene is at first formed, and this is converted by oxidation (which is partly spontaneous during the above reaction) into anthracene (B. **12**, 1965):



$$C_6H_4<^{Br}_{CH_2Br} + ^{BrCH_2}_{Br}>C_6H_4 + 4Na = C_6H_4<^{CH_2}_{CH_2}>C_6H_4 + 4NaBr;$$

$$C_6H_4<^{CH_2}_{CH_2}>C_6H_4 - H_2 = C_6H_4<^{CH}_{CH}>C_6H_4.$$

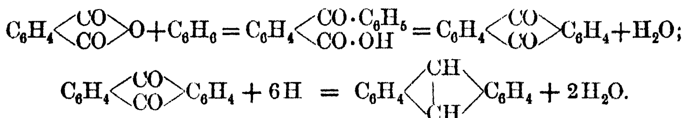
4. By heating benzene with symmetrical tetrabromo-ethane and aluminium chloride (*Anschutz*, B. **16**, 623):



$$C_6H_6 + \begin{matrix} BrCHBr \\ | \\ BrCHBr \end{matrix} + C_6H_6 = C_6H_4<^{CH}_{CH}>C_6H_4 + 4HBr.$$

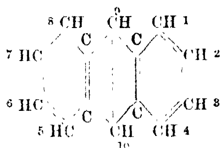
5. When phthalic anhydride is heated with benzene and aluminium chloride, *o*-benzoyl-benzoic acid is formed, and this when heated with phosphoric anhydride yields anthraquinone

(*Behr* and *v. Dorp*, B. **7**, 578), which on reduction with zinc dust gives anthracene:



6. When a mixture of *m*-xylene and styrene is treated with concentrated sulphuric acid, there is formed *α-tolyl-β-phenyl-propane*, $CH_3 \cdot C_6H_4 \cdot CH_2 \cdot CH <^{C_6H_5}_{CH_3}$, which decomposes almost quantitatively into methane, hydrogen, and methyl-anthracene when strongly heated (B. **23**, 3272).

Constitution.—From mode of formation 5, the anthracene molecule is seen to contain two benzene nuclei, C_6H_4, joined together by a middle group, C_2H_2. The carbon atoms of this middle group are likewise linked together, as is seen from mode of formation 4, and take up the *o*-position with regard to each other on one or other of the benzene nuclei (on one nucleus according to methods of formation 1 and 5, and on the other according to method 3; for further proofs of this, see *e.g. v. Pechmann*, B. **12**, 2124). The constitution of anthracene is thus the following (*Graebe* and *Liebermann*, A. Suppl. **7**, 313):



or possibly:



The two carbon atoms of the middle group thus form a new hexagon-ring with the carbon atoms of the benzene nuclei to which they are linked, so that anthracene may also be looked upon as being built up by the conjunction of three benzene nuclei. Besides the formula $C_6H_4 \langle {}^{CH}_{CH} \rangle C_6H_4$ (with the two CH groups joined), the "quinoid" formula $C_6H_4 \lll {}^{CH}_{CH} \rangle C_6H_4$ has also to be taken into consideration (*Armstrong*, P. 1890, 101; *Kehrmann*, B. 1894, **21**, 3348).

Properties and Behaviour.—Anthracene crystallizes in colourless plates which show a magnificent blue fluorescence. It is

insoluble in water and dissolves only sparingly in alcohol and ether, but readily in hot benzene. It melts at 213°, boils above 351°, and with picric acid yields an additive compound which crystallizes in beautiful red needles melting at 138°.

Anthracene is transformed by sunlight into the polymeric para-anthracene, $(C_{14}H_{10})_2$. When reduced with hydriodic acid and phosphorus it takes up, in the first instance, two atoms of hydrogen, with the formation of 9:10-dihydro-anthracene,

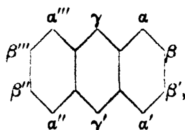


(see p. 537, mode of formation 3). This crystallizes in colourless plates, melts at 107°, and is readily soluble in alcohol. It sublimes readily and distils without decomposition, but yields anthracene at a red heat or when warmed with concentrated sulphuric acid.

Further addition of hydrogen yields the hydrides $C_{14}H_{16}$ and, finally, $C_{14}H_{24}$.

DERIVATIVES OF ANTHRACENE

Theoretically three isomeric mono-derivatives are possible in each case, viz., the α-, β-, and γ-compounds:



since in the graphical formula given on the preceding page, $1 = 4 = 5 = 8 = \alpha$, $2 = 3 = 6 = 7 = \beta$, and $9 = 10 = \gamma$. The observed facts are in complete accordance with this.

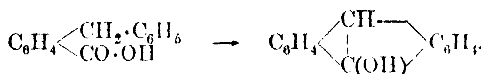
The position of the substituting group can usually be determined either by an examination of the oxidation products, *e.g.* if it be in the γ-position it will be eliminated and anthraquinone formed; or it is arrived at from the synthesis of the compound, *e.g.* in the case of alizarin, the formation of which from catechol and phthalic acid shows that its two hydroxyls are contained in one and the same benzene nucleus.

The number of di-substituted derivatives is large, for example, when both substituents are alike, 15 isomerides are theoretically possible.

Numerous derivatives of anthracene are known, *e.g.* halogen-, nitro-, amino-, and sulphonic acid derivatives.

Hydroxy-anthracenes.—The α- and β-compounds are termed α- and β-**anthrols**; they are obtained by fusing the corresponding sulphonic acids with alkali, and in their properties closely resemble phenols and naphthols.

γ-Hydroxy-anthracene or **anthranol** may be obtained by reducing anthraquinone with zinc and acetic acid, or synthetically, by the action of concentrated sulphuric acid on *o*-benzyl-benzoic acid at 80°:



It is readily oxidized to anthraquinone, and with hydroxylamine yields anthraquinone oxime.

Anthraquinone, $C_{14}H_8O_2$ (*Laurent*, 1834), is readily obtained by oxidizing anthracene with chromic acid mixture (which is the method followed on the large scale), or with chromic anhydride and glacial acetic acid, and is also produced when calcium benzoate is distilled.

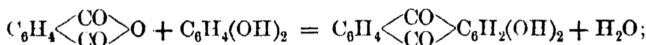
It crystallizes in yellow prisms or needles soluble in hot benzene, melts at 285°, sublimes with great readiness, and is exceedingly stable as regards oxidizing agents. Hydriodic acid at 150° reduces it either to anthracene or its dihydride, while fusion with potash converts it into benzoic acid. It possesses more of a ketonic than of a quinonic character (*Zincke*, *Fittig*), as it is not reduced by sulphurous acid, and gives an oxime with hydroxylamine.

It yields mono- and dibromo-, nitro- and sulphonic-acid derivatives. **Anthraquinone β-mono-sulphonic acid** crystallizes in yellow plates, and is formed by the action of sulphuric acid under normal conditions, but in the presence of mercury salts the isomeric α-acid is obtained; of the di-sulphonic acids two are formed directly from anthraquinone, and two may be prepared by the oxidation of the corresponding anthracene-disulphonic acids.

Fusion of the sulphonic acids with potash does not generally yield the analogous hydroxy-compounds in theoretical quantity, oxygen being usually absorbed from the air at the same time; thus the mono-sulphonic acids yield mono- and dihydroxy-, and the di-sulphonic acids di- and trihydroxy-anthraquinones. In practical working the theoretical amount of chlorate of

potash required is added to the "melt". Prolonged fusion with potash tends to form hydroxy-benzoic acids.

Various **hydroxy-anthraquinones** can also be prepared by the synthetical mode of formation 5, p. 537, viz., from phthalic anhydride and the mono- or dihydroxy-benzenes (*Baeyer* and *Caro*, B. **7**, 792; **8**, 152), *e.g.*:



$$C_6H_4<\begin{matrix}CO\\CO\end{matrix}>O + C_6H_4(OH)_2 = C_6H_4<\begin{matrix}CO\\CO\end{matrix}>C_6H_2(OH)_2 + H_2O;$$

phenol yields by this method the two hydroxy-anthraquinones (yellow needles), catechol yields alizarin, quinol yields quinizarin, and so on. The hydroxy-derivatives are further produced by fusing chloro- and bromo-anthraquinones with potash, while *m*-hydroxy-benzoic acid can be converted directly by sulphuric acid into anthraflavic acid, water being eliminated. Cf. A. **240**, 245.

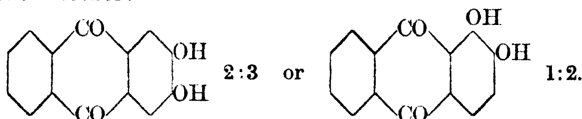
Alizarin, 1:2-dihydroxy-anthraquinone, $C_{14}H_8O_4$, is the most important constituent of the beautiful red dye of the madder root (*Rubia tinctorum*), which has been known for ages, being present in the latter as the readily decomposable glucoside, Ruberythric acid, $C_{26}H_{28}O_{14}$; in addition to alizarin, madder also contains purpurin. It is manufactured on the large scale by fusing anthraquinone-β-sulphonic acid with potassium hydroxide and chlorate (*Graebe* and *Liebermann*, *Caro*, *Perkin*, B. **3**, 359; A. **160**, 130).

It crystallizes in magnificent red prisms or needles of a glassy lustre, melts at 289°, and can be sublimed; it dissolves readily in alcohol and ether, only sparingly in hot water, but, as a phenol, very readily in alkalis to a violet-red solution. It yields insoluble coloured compounds—the so-called "**lakes**"—with metallic oxides, the alumina and tin lakes being of a magnificent red colour, iron lake violet-black, and lime lake blue. In the Turkey Red manufacture, for instance, the materials to be dyed are previously mordanted with acetate of alumina or with "ricinoleic-sulphuric acid".

Its constitutional formula is based on the following considerations:—(*a*) Its conversion into anthracene when heated with zinc dust (*Graebe* and *Liebermann*, B. 1868, **1**, 49; A. Sup. **7**, 297); (*b*) its formation by fusing dibromo-anthraquinone or anthraquinone-sulphonic acid with potash; (*c*) its synthesis from phthalic anhydride and catechol.

All these indicate that it is a dihydroxy-anthraquinone

with the two hydroxy-groups in the *o*-positions with respect to one another:



The fact that two isomeric mono-nitro-derivatives (with the nitro-group in the same nucleus as the two hydroxy-groups) have been prepared is a proof of the positions 1:2 for the hydroxy-groups.

Anthrarobin, *dihydroxy-anthranol*, $C_6H_4\left<\begin{matrix}C(OH)\\ | \\ CH\end{matrix}\right>C_6H_2(OH)_2$, obtained from alizarin, ammonia, and zinc dust, is a yellowish-white powder which yields alizarin on oxidation; on account of its reducing properties it is used in skin diseases.

Nitric peroxide converts alizarin into **β-nitro-alizarin** or alizarin orange, $C_{14}H_7(NO_2)O_4$, a yellowish-red dye; and this with glycerol and sulphuric acid (the *Skraup* reaction, p. 582), yields **alizarin blue**, $C_{17}H_9NO_4$ (see Quinoline), a valuable blue dye which is converted by fuming sulphuric acid into **alizarin green.**

For other examples of alizarine dyes see Chap. LV, I.

According to *v. Kostanecki* the colouring power of these compounds is connected with the presence of two hydroxyls in the ortho-position to one another.

The isomeric dihydroxy anthraquinones are known under the following names:—

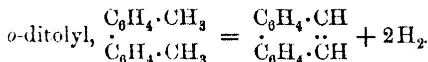
Quinizarine	...	...	...	=	1:4
Anthrarufine	...	...	...	=	1:5
Xanthopurpurine		...	...	=	1:3
Chrysazine	...	...	...	=	1:8
Hystazine	...	...	...	=	2:3
Anthraflavinic acid		...	...	=	2:6
Iso-anthraflavinic acid ...			...	=	2:7

B. Phenanthrene

Phenanthrene (*Fittig* and *Ostermeyer*, 1872, A. **166**, 361), which is isomeric with anthracene, accompanies this hydrocarbon in coal-tar. It crystallizes in colourless glistening

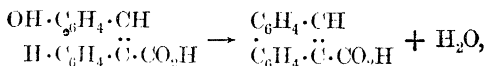
plates, dissolves in alcohol more readily than anthracene (yielding a blue fluorescent solution), melts at 99°, and boils at 340°. It may be separated from anthracene by partial oxidation and subsequent distillation, as the latter is more readily attacked. Oxidizing agents convert it into diphenic acid (p. 506). Its picrate crystallizes in yellow needles melting at 145°.

It may also be obtained:—1. By leading the vapour of toluene, stilbene, dibenzyl or *o*-ditolyl through a red-hot tube, thus:



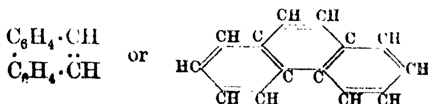
2. Together with anthracene from *o*-bromo-benzyl bromide and sodium.

3. *o*-Nitro-benzaldehyde with sodium phenyl-acetate and acetic anhydride (*Perkin's* synthesis, p. 470) yields α-phenyl-*o*-nitro-cinnamic acid, $NO_2\cdot C_6H_4\cdot CH{:}CPh\cdot CO_2H$, and when this is reduced, diazotized, and treated with copper powder, β-phenanthrene-carboxylic acid is formed,



and when carbon dioxide is eliminated this yields phenanthrene. (For other syntheses cf. *Pschorr*, B. 1896, **29**, 496; **32**, 162, 176; **33**, 496; *Rabe*, B. 1898, **31**, 1896; *F. Meyer* and *Balle*, A. 1914, **403**, 167.)

The formation of phenanthrene from *o*-ditolyl, and its oxidation to diphenic acid, $\begin{matrix} C_6H_4\cdot CO_2H \\ C_6H_4\cdot CO_2H \end{matrix}$, show that it is a diphenyl derivative, and that it contains a carbon atom linked to each benzene nucleus; this carbon atom is joined to the corresponding one by a double bond, as is shown, *e.g.*, by its formation from stilbene, $\begin{matrix} C_6H_5\cdot CH \\ C_6H_5\cdot CH \end{matrix}$, a reaction completely analogous to the preparation of diphenyl from benzene. Since diphenic acid is a di-ortho-diphenyl-dicarboxylic acid (*Schultz*, A. **196**, 1; **203**, 95), phenanthrene is also a di-ortho-derivative and possesses the following constitution:

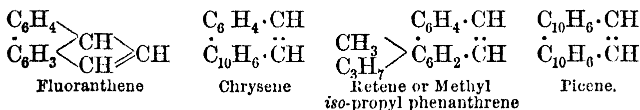


According to the above formula, the two CH-groups form a new hexagon ring with the carbon atoms of the two benzene nuclei to which they are linked, so that phenanthrene—like anthracene—may be looked upon as the product of the coalition of three benzene nuclei.

Additive and substitution products of phenanthrene are also known, *e.g.* a tetrahydride, nitro-, amino-, cyano-, and hydroxy-compounds, and sulphonic and carboxylic acids. **Phenanthrol**, $C_{14}H_9(OH)$, is a hydroxy-phenanthrene, and **phenanthrene-quinol**, $C_{14}H_8(OH)_2$, a dihydroxy-compound; when oxidized the latter yields phenanthraquinone, $\begin{matrix} C_6H_4\cdot CO \\ \vdots \quad\quad \vdots \\ C_6H_4\cdot CO \end{matrix}$, which may also be prepared directly from phenanthrene and chromic acid. It crystallizes in odourless, orange needles, melts at 200°, distils unchanged, and is not volatile in steam. Phenanthraquinone possesses the character of a diketone, reacting with hydroxylamine, sodium bisulphite, &c., but it can be reduced to the corresponding quinol by sulphurous acid. It gives a bluish-green coloration with toluene containing thio-tolene, glacial acetic acid, and sulphuric acid, and when the mixture is diluted and extracted with ether the latter becomes violet-coloured; this is the *Laubenheimer* reaction (B. **17**, 1338).

C. Complex Hydrocarbons

Fluoranthene, $C_{15}H_{10}$, **pyrene**, $C_{16}H_{10}$, **chrysene**, $C_{18}H_{12}$, **retene**, $C_{18}H_{18}$, and **picene**, $C_{22}H_{14}$, are hydrocarbons which have been isolated from that portion of coal-tar which boils above 360°. Phenanthrene, pyrene, and fluoranthene are also found in "Stupp" fat, *i.e.* the fat obtained as a by-product from the working up of mercury ores in Idria. They all crystallize in white plates, sublime without decomposition, and when oxidized are converted into the corresponding ketones.



Fluoranthene — Chrysene — Retene or Methyl *iso*-propyl phenanthrene — Picene.

(A. **240**, 147; **284**, 52; **351**, 218; B. **26**, 1745; B. **36**, 4200.)

Derivatives of complex hydrocarbons are formed by the action of $AlCl_3$ on oxy-derivatives of benzene, naphthalene, etc., *e.g.* 4:4′-diethoxy, 1:1-dinaphthyl from α-naphthyl ethyl ether (B. 1922, 324, 330).

HETEROCYCLIC COMPOUNDS

XXXIII. INTRODUCTION

The third great division of carbon derivatives consists of the *Heterocyclic Compounds*. These, like the carbocyclic compounds, contain a closed chain or ring, but differ from the latter by the presence in the actual ring of atoms of elements other than carbon (cf. formulæ, p. 546). The number of such compounds is enormous, although the number of elements usually associated with carbon in rings is comparatively small. The more common elements are oxygen and sulphur, but more especially nitrogen.

A number of these compounds have been already mentioned; among the oxygen compounds are ethylene oxide, glycolide, phthalic anhydride, and among the nitrogen compounds succinimide, phthalimide, and lactams.

The compounds are divided into groups according to the number of atoms constituting the ring, thus three-membered rings, *e.g.* ethylene oxide; four-membered rings, *e.g.* betaïne; five-membered rings, *e.g.* thiophene; six-membered rings, *e.g.* pyridine, &c. As in the carbocyclic series, the most important and also the most stable are the five- and six-membered rings. A further division of these groups can be made according to the *number* of atoms other than carbon present. Thus in the five-membered ring compounds we can have the following sub-groups: 4C + 1N; 3C + 2N; 2C + 3N; termed respectively the monazole, di- and tri-azole sub-groups.

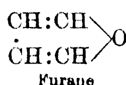
The stability of the compounds and their general chemical characteristics depend to a large extent on the saturated or unsaturated nature of the rings. Compounds like thiophene, pyrrole and pyridine are stable and closely resemble benzene—they possess general aromatic properties. Like benzene they can be reduced, the two former can each take up two or four atoms of hydrogen, and pyridine two, four or six. These reduction products no longer have aromatic properties. It is interesting to note that although the five-membered heterocyclic unsaturated compounds resemble benzene, the unsaturated carbocyclic compound cyclopentadiene does not.

Some of the common heterocyclic compounds contain condensed nuclei, *i.e.* the two condensed rings have two carbon atoms in common. A well-known example of condensed

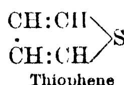
heterocyclic rings is met with in purine and its derivatives (p. 300). Examples of compounds containing a benzene nucleus condensed with a heterocyclic ring are met with in quinoline, coumarone and indole (see below).

Compounds with condensed nuclei behave very differently on oxidation. Certain of them have the heterocyclic ring ruptured, and thus yield ortho-derivatives of the carbon ring; others, again, have the carbon ring ruptured, and yield ortho-acids of the heterocyclic ring. The compounds dealt with in the following sections will be grouped as follows:

1. Five-membered heterocyclic compounds containing 4C + 1O, S or N atoms, or the **furane** group, *e.g.*:



Furane

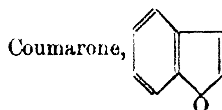


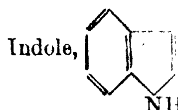
Thiophene



Pyrrole

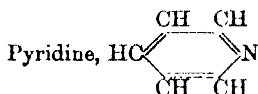
2. Compounds formed by the condensation of these rings with a benzene nucleus, *e.g.*:



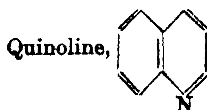


3. Five-membered heterocyclic compounds containing three carbon atoms, *e.g.* pyrazole and thiazole group.

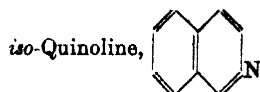
4. Six-membered heterocyclic compounds or **pyridine** group, *e.g.*:



5. The compounds formed by the condensation of a benzene and pyridine ring, *e.g.*:



and



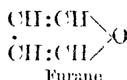
6. Six-membered heterocyclic compounds, with not more than four carbon atoms in the ring.

Within recent years compounds have been isolated which contain P, As, Sb, Bi, Si, Pb, Hg, Fe, Te, Se, or I as constituents of the ring. Most of these compounds are formed from 1:5-dibromopentane, $BrCH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2Br$, or 1:4 dibromobutane and derivatives of the element in question. Thus sodium amalgam and the 1:5-dibromo compound yield the product $CH_2 \begin{matrix} CH_2 \cdot CH_2 \\ CH_2 \cdot CH_2 \end{matrix} > Hg$ (B. 1914, **47**, 177, 186). The *Grignard* compound derived from 1:5-dibromopentane reacts with $SiCl_4$ or $SiMe_2Cl_2$, yielding the products $CH_2 < \begin{matrix} CH_2 \cdot CH_2 \\ CH_2 \cdot CH_2 \end{matrix} > SiCl_2$ and $CH_2 < \begin{matrix} CH_2 \cdot CH_2 \\ CH_2 \cdot CH_2 \end{matrix} > SiMe_2$ (B. 1915, **48**, 1236), or with $PbEt_2Cl_2$, yielding $CH_2 < \begin{matrix} CH_2 \cdot CH_2 \\ CH_2 \cdot CH_2 \end{matrix} > PbEt_2$ (B. 1916, **49**, 2666) as a colourless liquid, b.-pt. 110°/13·5 mm. The same *Grignard* reagent reacts with phenylphosphinedichloride, $C_6H_5 \cdot PCl_2$, yielding $CH_2 < \begin{matrix} CH_2 \cdot CH_2 \\ CH_2 \cdot CH_2 \end{matrix} > P \cdot C_6H_5$ (B. 1915, **48**, 1173).

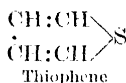
When the *Grignard* compound from 1:4-dibromobutane is condensed with $CH_3 \cdot PCl_2$, compounds of the type $\begin{matrix} CH_2 \cdot CH_2 \\ CH_2 \cdot CH_2 \end{matrix} > P \cdot CH_3$ are formed, and derivatives containing As, Sb, and Bi can be obtained by similar methods (B. 1916, **49**, 437).

These compounds are of no technical importance, but are of value from the theoretical point of view, and indicate the great variety of elements which can take part in ring formation.

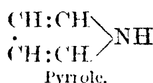
XXXIV. FURANE GROUP



Furane



Thiophene



Pyrrole.

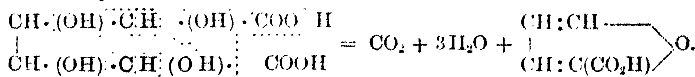
From these compounds a whole series of derivatives are obtained by the substitution of hydrogen by halogen, and also by the entrance of the groups $\cdot CH_3$, $\cdot CH_2OH$, $\cdot CHO$, $\cdot CO_2H$, &c. In their properties furane, thiophene, and pyrrole remind one of benzene. Thiophene, in particular, is delusively like the latter, *e.g.* in odour and boiling-point, and its various derivatives often show a marvellous similarity in their chemical and physical relations to the corresponding derivatives of benzene.

Furane, pyrrole, and thiophene also resemble one another in many respects. All three boil at relatively low temperatures (+ 32°, 131°, 84°), are either insoluble or only sparingly soluble in water, but readily in alcohol and ether, and show many analogous colour reactions. Thus pyrrole and thiophene and their derivatives give, for the most part, an intense violet to blue coloration when mixed with isatin and concentrated sulphuric acid, and a cherry-red or violet coloration with phenanthraquinone and glacial acetic or sulphuric acid. The vapour of pyrrole colours a pine shaving which has been moistened with hydrochloric acid carmine red (πυῤῥός, fiery-red), while furaldehyde vapour colours it an emerald green; the latter likewise colours a piece of paper moistened with xylidine- or aniline-acetate red. Furane is converted by mineral acids, *e.g.* hydrochloric acid, into an insoluble amorphous powder, and pyrrole into an insoluble amorphous brown-red powder, "pyrrole-red" (with evolution of ammonia), while thiophene remains unaltered. Pyrrole has feebly basic properties.

Just as benzene is formed by the pyrogenic polymerization of acetylene (p. 369), so several heterocyclic compounds are formed by the pyrogenic condensation of acetylene with H_2S or NH_3 (*R. Meyer* and *Wesche*, B. 1917, **50**, 422). In the former case thiophene and thionaphthalene are formed; also thiotolene if CH_4 is also present. In the latter case the products include pyrrole, pyridine, quinoline, in addition to aniline, naphthalene, fluorene, and anthracene.

Maleic anhydride (p. 255) is regarded by *Pfeiffer* and *Böttler* as the quinone of furane, $\begin{matrix} CH \cdot CO \\ \ddot{} \\ CH \cdot CO \end{matrix} > O$; as such it yields coloured additive compounds with arylamines, phenols, phenolic ethers, and complex aromatic hydrocarbons (B. 1918, **51**, 1819).

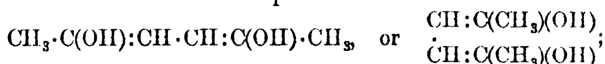
Derivatives of all three compounds may be obtained from mucic acid, $CO_2H \cdot (CH \cdot OH)_4 \cdot CO_2H$ (p. 268). When distilled, mucic acid yields pyromucic acid or furane-α-carboxylic acid; when its ammonium salt is distilled, pyrrole is formed; and when free mucic acid is heated with barium sulphide, thiophene α-carboxylic acid is obtained, *e.g.*:



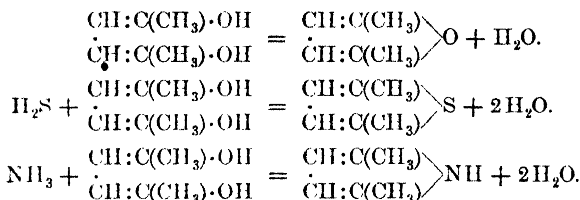
Pyrrole derivatives are also formed by condensing β-ketonic esters (p. 234) with amino-ketones (A. 1916, **411**, 350).

A very general method for the formation of derivatives of this group is from γ-diketones, *e.g.* acetonyl-acetone, $CH_3 \cdot CO \cdot CH_2 \cdot CH_2 \cdot CO \cdot CH_3$ (p. 229; also p. 238). When this compound is heated with phosphorus pentoxide or zinc chloride, dimethyl-furane is formed; with phosphorus pentasulphide, dimethyl-thiophene; with alcoholic ammonia, dimethyl-pyrrole (B. 18, 58, 367; 20, 1074).

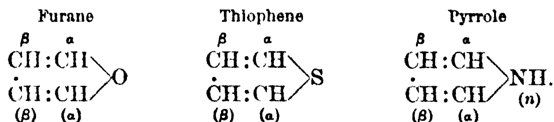
This behaviour would indicate that the acetonyl-acetone reacts as the tautomeric compound:



upon this assumption the formation of dimethyl-furane appears simply as that of an anhydride, that of dimethyl-pyrrole as an exchange of 2(OH) for NH (imide formation), and that of dimethyl-thiophene as the formation of a sulphide, *i.e.* exchange of 2(OH) for S, according to the following equations:



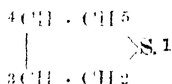
From the above reactions the *constitutional formulæ* for the three compounds would be:



These formulæ receive corroboration from the frequently observed fact that the substances are capable of yielding additive compounds with bromine or hydrogen (see Pyrroline). According to the above formulæ, two isomeric mono-substituted derivatives of furane and thiophene are possible: (1) one in which the hydrogen atom (α) which stands nearest to the oxygen, sulphur, or nitrogen atom, and (2) one in which a quasi-middle hydrogen atom (β) is substituted. As a matter

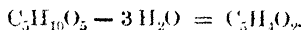
of fact, two such isomers have been observed in many cases, *e.g.* two thiophenic acids. These form mixed crystals, the crystals having a homogeneous appearance although they contain both acids (*V. Meyer*, A. 236, 200). In the case of pyrrole, on the other hand, three kinds of derivatives (α-, β-, and n-) are both possible and known.

An examination of the molecular refraction of thiophene and also of its heat of combustion (B. 1885, 18, 1832) point to the presence of only one double bond in the thiophene molecule. The formula $\begin{matrix} CH\cdot CH \\ \vdots \quad\ \vdots \\ CH\cdot CH \end{matrix}\!\!>\!S$ has been suggested, and this is quite in harmony with the production of substituted maleic acids by the oxidation of thiophene derivatives. Probably the simplest explanation is that the thiophene molecule contains centric bonds, and should be represented as:



Furane or **furfurane** is a colourless mobile liquid, boiling at 32°, and with an odour resembling that of chloroform. It is present in pine-wood tar, in the first runnings from ordinary wood tar, &c., and is obtained by the distillation of sugar with lime, or by distilling barium pyromucate. α-**Methyl-furane** or *sylvane* is likewise present in pine-wood tar, and in the products of distillation of sugar with lime. It boils at 65°. $\alpha\alpha$-**Dimethyl-furane** is obtained from sugar and lime, and also from acetonyl-acetone (p. 549). It is a colourless mobile liquid of a characteristic odour, and boils at 94°. Concentrated acids convert it into a resin; it can be transformed back into acetonyl-acetone.

Furol, *α-furaldehyde* or *furfuraldehyde*, $C_4H_3O\cdot CHO$ (*Döbereiner*), is obtained when pentoses, *e.g.* arabinose and xylose or the complex pentosans are distilled with concentrated hydrochloric acid:



$$C_5H_{10}O_5 - 3\,H_2O = C_5H_4O_2.$$

The yield is quantitative, and the method is made use of for determining the amounts of pentoses present in various substances. It may also be obtained by distilling bran, wood, sugar, or various carbohydrates with moderately concentrated sulphuric acid. It is a colourless oil of agreeable odour, turns

brown in the air, and boils at 162°. It is manufactured on an appreciable scale as a solvent.

It possesses all the properties of an aldehyde, and can yield condensation products in much the same manner as benzaldehyde (p. 453): *e.g.* **furoïn**, $C_4H_3O \cdot CH(OH) \cdot CO \cdot C_4H_2O$, corresponding with benzoin; **furalmalonic acid**, $C_4H_8O \cdot CH:C(CO_2H)_2$, corresponding with benzalmalonic acid; and **furylacrylic** and *allo*-**furylacrylic acid**, $C_4H_3O \cdot CH:CH \cdot CO_2H$, corresponding with cinnamic and *allo*-cinnamic acids.

Pyromucic acid, $C_4H_3O \cdot CO_2H$.—Furane-α-carboxylic acid crystallizes in needles or plates similar to those of benzoic acid, and melts at 132°; it sublimes easily, is readily soluble in hot water and alcohol, and decolorizes alkaline permanganate almost instantaneously.

Pyrrole is a constituent of coal-tar (*Runge*) and of bone-oil (*Anderson*); it boils at 131°, and possesses, like many of its homologues, a chloroform odour. It is a secondary base, and its imino-hydrogen is replaceable by metals and alkyl, or acyl radicals.

In addition to the methods of formation mentioned on p. 549, it may also be obtained by heating succinimide (p. [illegible]47) with zinc dust, or from acetylene and ammonia at a red heat.

When pyrrole is acted upon by hydroxylamine the ring is broken, and the dioxime of succinic-aldehyde,

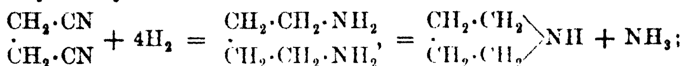
$$\begin{array}{l} CH_2 \cdot CH:N \cdot OH \\ \vert \\ CH_2 \cdot CH:N \cdot OH \end{array},$$

is formed; this yields tetramethylene-diamine upon reduction (B. **22**, 1968). Dimethyl-pyrrole in a similar manner yields acetonyl-acetone-dioxime.

n-**Potassium-pyrrole**, C_4H_4NK, which is obtained from pyrrole and potassium or solid potassic hydroxide, is a colourless compound which is decomposed by water. A number of *n*-alkyl and acyl derivatives may be prepared by the aid of this potassium compound, but most of them are relatively unstable, and when heated are transformed into the isomeric *a*-alkyl or acyl compounds. A most interesting reaction is the conversion of pyrrole into pyridine (p. 570) by means of sodium methoxide and chloroform or methylene iodide. By the action of iodine and alkali, substitution takes place with the formation of **tetra-iodo-pyrrole** or **iodole**, $C_4I_4(NH)$, which crystallizes in yellow plates, and is used as an antiseptic in place of iodoform.

Zinc and glacial acetic acid convert pyrrole into **pyrroline**,

$\begin{matrix} CH:CH- \\ CH_2\cdot CH_2 \end{matrix}\!\!>\!NH$, or more probably $\begin{matrix} CH\cdot CH_2 \\ \vdots \\ CH\cdot CH_2 \end{matrix}\!\!>\!NH$ (B. 1901, **34**, 3954), a colourless liquid boiling at 91° and also a strong secondary base; when this latter is heated with hydriodic acid, it is further reduced to **pyrrolidine**, $\begin{matrix} CH_2\cdot CH_2 \\ \cdot \\ CH_2\cdot CH_2 \end{matrix}\!\!>\!NH$, a colourless, strongly alkaline base resembling piperidine, and boiling at 86°. It is also formed by the action of sodium on an alcoholic solution of succinimide, and is obtained synthetically by heating δ-chloro-butylamine with alkali, and by treating ethylene cyanide with sodium and alcohol, thus:



$$\begin{matrix} CH_2\cdot CN \\ \cdot \\ CH_2\cdot CN \end{matrix} + 4H_2 = \begin{matrix} CH_2\cdot CH_2\cdot NH_2 \\ \cdot \\ CH_2\cdot CH_2\cdot NH_2 \end{matrix}, = \begin{matrix} CH_2\cdot CH_2 \\ \cdot \\ CH_2\cdot CH_2 \end{matrix}\!\!>\!NH + NH_3;$$

it is consequently designated **tetramethylene-imine** (*Ladenburg*).

Pyrrole forms complex condensation products with acetone and other ketones. These products probably contain 4-pyrrole nuclei attached to one another in the α-positions by means of CMe_2 groups.

The red colouring matter of blood yields pyrrole derivatives as some of its products of decomposition, *e.g.* β-ethyl-*ααβ*-trimethyl- and β-ethyl-*αβ*-dimethyl pyrrole (B. **44**, 2758), and pyrrolidine derivatives, especially pyrrolidine-carboxylic acid (proline), are decomposition products of albumen.

Thiophene (*V. Meyer*, B. **16**, 1465, &c.) is present in coal-tar, being invariably found in benzene (up to 0·5 per cent.); the same applies to its homologues thiotolene (methyl-thiophene), and thioxene (dimethyl-thiophene), which accompany toluene and xylene, &c. Its boiling point (84°) is almost the same as that of benzene (80·4°), from which it is extracted by repeatedly shaking with small quantities of concentrated sulphuric acid, which transforms the thiophene into a soluble sulphonic acid (B. **17**, 2641, 2852). It is also attacked more readily than benzene by other reagents, such as halogens.

Thiophene is also obtained synthetically by leading the vapour of ethyl sulphide through a red-hot tube (*Kekulé*), in small quantity by heating crotonic acid, *n*-butyric acid, paraldehyde, with phosphorus pentasulphide, and in fairly large quantities by passing acetylene over iron pyrites heated to 300° (*Steinkopf*, A. 1914, **403**, 1), or even better from a mixture of acetylene and H_2S over alumina at about 400° (Abs. 1915, i, 638).

Stilbene (p. 510) and sulphur yield **tetraphenylthiophene,** *thionessal*, m.-pt. 183°.

The preparation and properties of the thiophene derivatives are almost identical with those of the corresponding benzene compounds. Thus nitric acid acts on thiophene to produce a **nitro-thiophene,** analogous to nitro-benzene, which can in its turn be reduced to amino-thiophene; the latter is, however, much less stable than the corresponding amino-benzene.

The boiling-points of thiophene compounds and their corresponding benzene derivatives are almost identical.

The homologues can be obtained by *Fittig's* synthesis, the α-compounds from 1:4-diketones, and the β-derivatives from mono- or di-substituted succinic acids and phosphorus pentasulphide.

Thiophene-sulphonic acid, $OH \cdot SO_2 \cdot C_4H_3S$, decomposes into thiophene and sulphuric acid when superheated with water, and does not yield a phenol on fusion with potash.

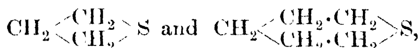
Hydroxythiotolene, $C_4H_2S(CH_3)(OH)$, the phenol of thiotolene, is formed by heating lævulic acid with P_2S_5 (B. **19**, 553).

A mixture of the α- and β-monocarboxylic acids when crystallized slowly from water yields **mixed crystals,** which cannot be resolved into their components.

The sulphur atom in thiophene is somewhat inert, but hydrogen peroxide converts tetraphenylthiophene into the **sulphone** $C_4Ph_4 \cdot SO_2$.

Tetrahydrothiophene can be synthesised from 1:4-dibromobutane and sodium sulphide. It is a colourless liquid with an intense odour, boils at 118° and readily yields a sulphone.

The cyclic compounds,



$$CH_2<\begin{matrix}CH_2\\CH_2\end{matrix}>S \text{ and } CH_2<\begin{matrix}CH_2 \cdot CH_2\\CH_2 \cdot CH_2\end{matrix}>S,$$

which are homologues of tetrahydrothiophene can be synthesised in a similar manner, and in properties closely resemble the alkyl sulphides R_2S (p. 91). The ring can be ruptured and unsaturated compounds formed by first forming the sulphonium salt, *e.g.* addition of methyl iodide and subsequent treatment with alkali, a reaction analogous to the exhaustive methylation of nitrogen compounds. (J. russ. 1916, **48**, 880-974.)

Ketones derived from thiophene are also known, *e.g.* 2-**acetylthiophene** from acetylchloride and thiophene-2-mercurichloride (A. 1914, **403,** 50).

A compound containing two condensed thiophene nuclei

CMe · C · CMe
C̈H C̈ C̈H
S S

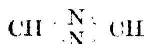
is formed by heating *n*-octane and sulphur at high temperatures. (*Friedmann*, B. 1916, **49**, 1344.)

Four membered rings containing two nitrogen or two sulphur atoms are known.

The following system of nomenclature has been suggested for the nitrogen compounds:


Uretidine


Uretidone

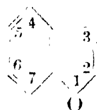

Urete


Uretine


Uretone.

One of the simplest members is 1:4-**diphenyluretidone**, needles decomposing at 224° and formed by the action of a cold concentrated solution of potassium cyanate on benzaldazine (p. 455) in glacial acetic acid (*Hale*, J. A. C. S. 1919, **41**, 370).

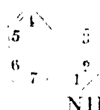
XXXV. COMPOUNDS FORMED BY THE CONDENSATION OF A BENZENE NUCLEUS WITH A FURANE, THIOPHENE, OR PYRROLE RING



Coumarone



Benzo-thiophene



Indole.

A. **Coumarone** occurs in coal-tar, and may be isolated as its **picrate**. It is usually obtained from bromocoumarin; this with alcoholic potash yields coumarilic acid, which gives coumarone when distilled with lime:



$$C_6H_4\langle{}^{CH:CBr}_{O-CO} \rightarrow C_6H_4\langle{}^{CH=}_{O-}\rangle C\cdot CO_2H \rightarrow C_6H_4\langle{}^{CH}_{O}\rangle CH.$$

It is a colourless liquid distilling at 170°; yields a **dibromide** and a **dihydro**-derivative, thus indicating the presence of a double bond. A 30–40 per cent yield of **coumaran**, $C_6H_4\langle{}^{CH_2}_{O-}\rangle CH_2$, is obtained by heating phenyl β-bromoethyl ether, $C_6H_5\cdot O\cdot CH_2\cdot CH_2Br$, from ethylene dibromide and sodium phenoxide, with $ZnCl_2$. (J. A. C. S. 1919, **41**, 648.)

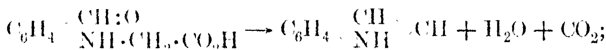
Benzo-thiophene, *Thionaphthene,* melts at 31°, boils at 221°, and has an odour resembling naphthalene.

B. INDOLE GROUP

Indole (*Baeyer*, 1868) is the most important compound in this group, as it is the parent substance of indigo. As a derivative of pyrrole it possesses feebly basic properties. It is obtained by distilling oxindole with zinc dust; by heating *o*-nitro-cinnamic acid with potash and iron filings; by the action of sodium ethoxide upon *o*-amino-β-chloro-styrene (B. **17,** 1067):



by the elimination of water and carbon dioxide from *o*-aldehydo-phenylglycine under the influence of acetic anhydride:



or by the pancreatic fermentation of albumen; together with skatole by fusing albumen with potash; and by passing the vapours of various anilines, *e.g.* diethyl-*o*-toluidine, through red-hot tubes, &c. It occurs in the essential oil of jasmine flowers, crystallizes in plates, melts at 52°, volatilizes readily with steam, and usually has a peculiar fæcal-like odour, although in the pure state and diluted it is stated to have a fragrant odour. It is feebly basic, colours a pine shaving which has been moistened with hydrochloric acid cherry-red, with nitrous acid gives a red precipitate, which consists partly of the so-called nitroso-indole, $[C_8H_6N(NO)]_2$ (a delicate reaction; see B. **22,** 1976), and yields acetyl-indole when acetylated. These last reactions show that indole contains an imino-group. When oxidized with ozone it yields indigo.

The system of numbering the substituents in the indole molecule is given on p. 554. The 1-substituted derivatives are sometimes termed *n*-derivatives, *e.g.* *n*-methyl-indole,



Various derivatives may be obtained synthetically by the condensation of the aromatic primary or secondary hydrazines either with pyroracemic acid or with certain ketones or aldehydes, and treatment of the resulting hydrazones with dilute hydrochloric acid or zinc chloride, when ammonia is eliminated

(*E. Fischer*, A. 236, 116; 242, 372); thus acetone-phenyl-hydrazone, $C_6H_5\cdot NH\cdot N:C<^{CH_3}_{CH_3}$, yields 2-methyl-indole, $C_6H_4<^{NH}_{CH}>C\cdot CH_3$, propaldehyde-phenyl-hydrazone yields skatole, and phenacyl bromide and aniline yield 2-phenyl-indole. See also B. 25, 2860.

Skatole, *3-methyl-indole*, $C_6H_4<^{NH}_{CMe}>CH$, is found in fæces, and is produced, together with indole, *e.g.*, by the decay of albumen, or by fusing it with potash. It crystallizes in colourless plates of a strong fæcal odour and melts at 95°. Nitrous acid does not colour it red. It takes up two atoms of hydrogen to form a hydro-compound. Acids, aldehydes, &c., are also known.

Dioxindole, $C_6H_4<^{CH(OH)}_{NH}>CO$, or the lactam of *o*-amino mandelic acid, $NH_2\cdot C_6H_4\cdot CH(OH)\cdot CO_2H$, is obtained by the reduction of isatin (into which it is again easily oxidized) with zinc dust and hydrochloric acid, or by the oxidation of oxindole. It crystallizes in colourless prisms, melts at 180°, and possesses both basic and acid properties (two hydrogen atoms being replaceable); it also forms a nitroso-compound, an N-acetyl derivative, &c.

Oxindole, $C_6H_4<^{NH}_{CH_2}>CO$, the lactam of *o*-amino-phenyl-acetic acid, is formed by the reduction of *o*-nitro-phenyl-acetic acid (p. 482); also by that of dioxindole with tin and hydrochloric acid. It crystallizes in colourless needles, melts at 120°, is readily oxidized to dioxindole, and therefore possesses feebly reducing properties. Oxindole is amphoteric, dissolving both in alkalis and in hydrochloric acid. Baryta water at a somewhat high temperature transforms it into barium *o*-amino-phenyl-acetate. The imino-hydrogen is exchangeable for ethyl, acetyl, the nitroso-group, &c.

Isomeric with oxindole is **indoxyl**, $C_6H_4<^{C(OH)}_{NH}>CH$, which is obtained by the elimination of carbon dioxide from indoxylic acid, a product formed from phenyl-glycocoll (p. 482), also by fusing indigo with potash. It is often present in the urine of the carnivora as potassium indoxyl-sulphate or urine-indican, $C_8H_6N\cdot O\cdot (SO_3K)$. It forms yellow crystals, melting at 85°, is moderately soluble in water with yellow fluorescence, and

not volatile with steam. It is very unstable, quickly becoming resinous, and is readily transformed into indigo when its alkaline solution is exposed to the air, or when ferric chloride is added to its solution in hydrochloric acid.

It yields a nitroso-compound, $C_6H_4<{N(NO) \atop C(OH)}>CH$, of the same character as the nitrosamines, and therefore it contains an imino-group; further, its relation to indoxyl-sulphuric acid shows that it contains an alcoholic hydroxy-group, and thus its constitution follows.

Potassium indoxyl-sulphate is prepared synthetically by warming indoxyl with potassium pyrosulphate; it crystallizes in glistening plates and is hydrolysed when warmed with acids.

Ethyl-indoxyl is obtained from indoxyl by the exchange of the hydroxylic hydrogen for C_2H_5. Derivatives of the hypothetical **pseudo-indoxyl**, $C_6H_4<{NH \atop CO}>CH_2$, are also known, some of them being convertible into indigo derivatives (*e.g* diethyl-indigo).

Indoxylic acid, $C_6H_4<{NH \atop C(OH)}>C \cdot CO_2H$, the carboxylic acid of indoxyl, forms white crystals, is oxidized to indigo by ferric chloride, and breaks up into indoxyl and carbon dioxide when fused. It is obtained from its ester, **ethyl indoxylate**, by fusing with soda. The latter compound crystallizes in stout prisms, melts at 120°, and may be obtained, among other methods, by the reduction of ethyl *o*-nitro-phenyl-propiolate with ammonium sulphide.

Isatin, $C_6H_4<{CO \atop NH}>CO$, the lactam of *o*-amino-benzoyl-formic acid (p. 493), is readily prepared by oxidizing indigo or indoxyl with nitric acid (*Erdmann* and *Laurent*, 1841; cf. also B. 17, 976). It may also be obtained by the oxidation of dioxindole or of oxindole (indirectly).

The following are among some of the most important methods by means of which isatin has been synthesised:—

(*a*) When *o*-nitro-phenyl-glyoxylic acid (*o*-nitro-benzoyl-formic acid, p. 493) is reduced, the corresponding amino-acid is obtained; but this immediately loses water, yielding a lactam or lactim:

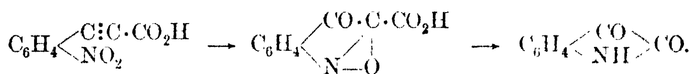


$$C_6H_4<{CO \cdot CO \cdot OH \atop NH_2} \rightarrow C_6H_4<{CO \atop NH}>CO \text{ or } C_6H_4<{CO \atop N}>C \cdot OH.$$

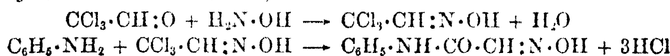
(*b*) *o*-Nitro-phenylacetic acid when reduced yields the lactam, oxindole, $C_6H_4<\genfrac{}{}{0pt}{}{CH_2}{NH}>CO$, and this with nitrous acid gives the iso-nitroso-oxindole, $C_6H_4<\genfrac{}{}{0pt}{}{C(:N\cdot OH)}{NH}>CO$, which on reduction is converted into amino-oxindole, and this on oxidation with ferric chloride yields isatin.

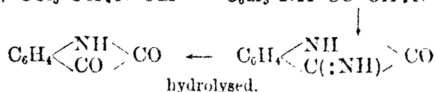
(*c*) *Sandmeyer* has worked out the following synthesis:—Aniline and carbon disulphide readily yield thio-carbanilide, $CS(NHC_6H_5)_2$, which, on boiling with potassium cyanide, white-lead, and water, yields hydrocyano-carbo-diphenylimide, $C_6H_5\cdot N:C(CN)\cdot NHC_6H_5$. With ammonium sulphide this latter yields $\genfrac{}{}{0pt}{}{NH_2\cdot CS}{C_6H_5\cdot N}>C\cdot NHC_6H_5$, which is converted by concentrated sulphuric acid into α-isatin-anilide, $C_6H_4<\genfrac{}{}{0pt}{}{CO}{N=}>C\cdot NHC_6H_5$, and this may be hydrolysed by dilute acids to isatin and aniline (C.C. 1900, **2**, 928).

(*d*) *o*-Nitrophenyl-propiolic acid (p. 486) may be synthesised, and when this is warmed with alkalis it undergoes molecular rearrangement and yields **isatogenic acid**, which by elimination of carbon dioxide forms isatin:



(*e*) Isatin and its homologues are readily formed by condensing aniline or substituted anilines with a freshly prepared solution of hydroxylamine sulphate and chloral hydrate (*Sandmeyer*, Helv. 1919, **2**, 234).



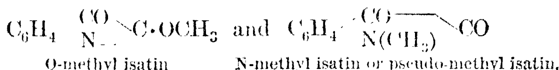


or (*f*) By internal condensation of substituted oxamic chlorides, *e.g.* $C_6H_5NR\cdot CO\cdot CO\cdot Cl$ with $AlCl_3$. (*Stollé*, B. 1913, 3915; J. pr. 1922, [2], **105**, 137,

Isatin crystallizes in reddish-yellow prisms, sparingly soluble in cold water, but more readily in hot water or alcohol. It dissolves in potassium hydroxide solution, yielding the potassium derivative, $C_6H_4<\genfrac{}{}{0pt}{}{CO}{N=}>C\cdot OK$, which is readily hydrolysed to

potassium *o*-amino-phenyl-glyoxylate when boiled with water. **Isatin chloride,** $C_6H_4<\genfrac{}{}{0pt}{}{CO}{N}>C\cdot Cl$, is obtained when isatin is heated with phosphorus pentachloride, and on reduction with zinc dust and acetic acid yields indigo.

Two isomeric methyl ethers are known:



The O-ether is obtained by converting potassium-isatin into the silver compound, and then heating this with methyl iodide. It is a colourless solid melting at 102°, and on hydrolysis yields isatin or *o*-amino phenyl-glyoxylic acid.

The N-ether may be obtained by the action of sodium hypobromite on N-methyl-indole. Its constitution follows from its method of formation, and also from the fact that on hydrolysis it yields *o*-methylamino-phenyl-glyoxylic acid, $C_6H_4<\genfrac{}{}{0pt}{}{CO\cdot CO_2H}{NHCH_3}$.

The constitution of isatin itself for some years was a matter of dispute; from its method of formation it must be either the lactam or lactim of *o*-amino-phenyl-glyoxylic acid. The examination of its absorption spectrum has established its lactam structure (Chap. XLVII, G.).

C. INDIGO AND RELATED COMPOUNDS

Indole or benzo-pyrrole	$C_6H_4<\genfrac{}{}{0pt}{}{CH}{NH}>CH.$
Indoxyl or hydroxy-indole	$C_6H_4<\genfrac{}{}{0pt}{}{C(OH)}{NH}>CH.$
Oxindole or *o*-amino-phenyl-acetic acid lactam	$C_6H_4<\genfrac{}{}{0pt}{}{CH_2}{NH}>CO.$
Dioxindole or *o*-amino-mandelic acid lactam	$C_6H_4<\genfrac{}{}{0pt}{}{CH(OH)}{NH}>CO.$
Isatin or *o*-amino-phenyl-glyoxylic acid lactam	$C_6H_4<\genfrac{}{}{0pt}{}{CO}{NH}>CO.$
Indigo	$C_6H_4<\genfrac{}{}{0pt}{}{CO}{NH}>C:C<\genfrac{}{}{0pt}{}{CO}{NH}>C_6H_4.$

Indigo, which is obtained from the indigo plant (*Indigofera tinctoria*), and from woad (*Isatis tinctoria*), has been known for thousands of years as a valuable blue dye, especially for woollen fabrics. In addition to indigo-blue (indigotin),

commercial indigo contains indigo-gelatine, indigo-brown, and indigo-red, all of which can be extracted from it by solvents. The colouring matter is not present as such in the indigo plant, but as the glucoside of indoxyl "Indican", from which it can be prepared either by dilute acids or certain enzymes and subsequent oxidation with atmospheric oxygen.

It forms a dark-blue coppery and shimmering powder or, after sublimation, copper-red prisms, insoluble in most solvents (including the alkalis and dilute acids), but dissolving to a blue solution in hot aniline and to a red one in paraffin, from either of which it may be crystallized. Its vapour is dark-red. The formula $C_{16}H_{10}O_2N_2$ is confirmed by its vapour density. It is converted by reducing agents, such as ferrous sulphate and caustic soda solution or grape-sugar and soda, into the leuco-compound, indigo-white, $C_{16}H_{12}O_2N_2$, a white crystalline powder soluble in alcohol and ether, also in alkalis (as a phenol); the alkaline solution quickly becomes oxidized by the oxygen of the air, with the separation of a blue film of indigo. It yields an acetyl compound which crystallizes in colourless needles.

Warm concentrated or fuming sulphuric acid dissolves indigo to indigo-monosulphonic and disulphonic acids, the former of which (termed phœnicin-sulphonic acid) is sparingly soluble in water, but the latter readily so; the sodium disulphonate is the indigo-carmine of commerce. Nitric acid oxidizes indigo to isatin, while distillation with potash yields aniline, and heating with manganese dioxide and a solution of potash, anthranilic acid.

Indigo has been prepared synthetically by numerous methods. The following are among the most important:—

1. By the reduction of isatin chloride with zinc dust and acetic acid:



$$2C_6H_4\Big\langle{CO \atop N}\Big\rangle CCl + 4H = C_6H_4\Big\langle{CO \atop NH}\Big\rangle C:C\Big\langle{CO \atop NH}\Big\rangle C_6H_4 + 2HCl.$$

The syntheses of isatin already described (pp. 557 and 558) are thus syntheses of indigo.

2. By warming *o*-nitro-phenyl-propiolic acid with grape-sugar in alkaline solution (*Baeyer*, 1880):



$$2NO_2\cdot C_6H_4C:C\cdot CO_2H + 4H = C_{16}H_{10}N_2O_2 + 2CO_2 + 2H_2O.$$

3. *Baeyer* and *Drewson* (1882) started with toluene, and on nitration obtained a mixture of *o*- and *p*-nitro-toluenes. The

o-compound was oxidized by manganese dioxide and sulphuric acid to *o*-nitro-benzaldehyde, and this was then condensed with acetone, yielding *o*-nitro-phenyl-lactyl methyl ketone,



$$NO_2 \cdot C_6H_4 \cdot CH(OH) \cdot CH_2 \cdot CO \cdot CH_3;$$

which when warmed with alkalis gave indigo and water. The yield was good, but the method was of no great practical importance, as the amount of toluene is limited, and no use could be found for the *p*-nitro-toluene obtained as a by-product.

4. In 1890 *Heumann* obtained **phenyl-glycocoll** by the condensation of aniline with chloracetic acid:



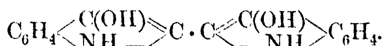
$$C_6H_5 \cdot NH\ H + Cl\ \cdot CH_2 \cdot CO_2H \rightarrow C_6H_5 \cdot NH \cdot CH_2 \cdot CO_2H,$$

and when this was fused with alkali, indigo-white was obtained.

A modified form of *Heumann's* synthesis consists in condensing anthranilic acid (p. 482) with chloracetic acid, when phenyl-glycocoll-*o*-carboxylic acid is obtained, and this on fusion with alkali yields indoxyl, which oxidizes in the air to indigo-blue. The yield is good, and this method is now employed on a manufacturing scale by the "Badische Anilin Fabrik" for the production of artificial indigo, as anthranilic acid can be obtained cheaply; the general method being the oxidation of naphthalene by mercury and sulphuric acid to phthalic acid, the conversion of this into phthalic anhydride, and then into phthalimide by the aid of ammonia. The phthalimide with alkali and chlorine yields anthranilic acid—*o*-amino-benzoic acid (*Hofmann* reaction, p. 191).

For homologues and derivatives, cf. Chap. LV, K.

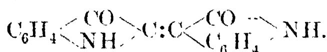
Indigo-blue is a very valuable blue dye, on account of its "fastness" to light, alkalis, acids, and soaps. As indigo-blue itself is insoluble, its "leuco" compound indigo-white is usually employed, the fabric being immersed in an alkaline solution of this, and then exposed to the air, when oxidation to indigo-blue takes place. Indigo-blue is usually reduced to indigo-white by means of calcium hyposulphite or by glucose and caustic soda. The indigo-white is a colourless solid with phenolic properties, and probably has the constitution represented in the formula—



$$C_6H_4 {<}{\genfrac{}{}{0pt}{}{C(OH)}{NH}}{>} C \cdot C {<}{\genfrac{}{}{0pt}{}{C(OH)}{NH}}{>} C_6H_4.$$

Indirubin, *Indigo-purpurin*, is an isomeride of indigo-blue,

and can be obtained synthetically by the condensation of isatin and indoxyl in alkaline alcoholic solution:



It is also obtained, together with indigo-blue, by the reduction of isatin chloride. It crystallizes from aniline in chocolate-brown needles, and on oxidation yields isatin.

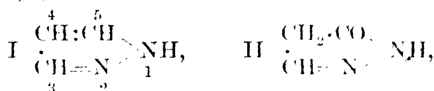
(For history and manufacture of indigo, see J. Ind. 1901, 239, 332, 551, 802; J. C. S. 1905, 974.)

XXXVI. PYRAZOLE GROUP, ETC.

1. PYRAZOLE GROUP

This comprises compounds with a five-membered ring containing three carbon and two nitrogen, sulphur, or oxygen atoms.

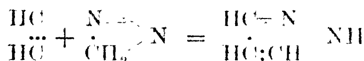
Pyrazole (I),



is theoretically derivable from pyrrole in the same way as pyridine is from benzene, *i.e.* by the exchange of CH for N.

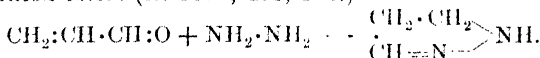
The positions three and five appear to be identical unless the H of the NH is replaced by alkyl groups.

It is a weak base of great stability, crystallizing in colourless needles; it melts at 70°, boils at 185°, and possesses aromatic properties (B. 1895, **28**, 714). Its simplest synthesis is by the union of acetylene and diazo-methane:



(*Von Pechmann*, B. 1897, **31**, 2950; see also B. **23**, 1103; A. **273**, 214.)

Pyrazoline, $C_3H_6N_2$, and **pyrazolidine**, $C_3H_8N_2$, are reduction products of pyrazole. Pyrazoline derivatives can be synthesised by condensing hydrazines with α-olefinic aldehydes or ketones. (B. 1918, 1457) or aliphatic diazo compounds with unsaturated esters (A. 1929, **470**, 284.)

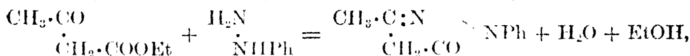


Characteristic of many of these pyrazoline derivatives is the

readiness with which they give up nitrogen when heated and yield corresponding derivatives of trimethylene (*Kishner*, Abs. 1912, i, 245; 1913, i, 1163; 1916, i, 290).

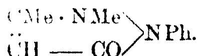
Pyrazolone (II) is an oil boiling at 77°.

1-Phenyl-3-methyl-pyrazolone is obtained by the action of phenylhydrazine on ethyl acetoacetate (p. 238),



crystallizes in compact prisms, melts at 127°, and boils without decomposition. As a weak base it dissolves in acids, but is also soluble in alkalis; it further contains the chemically-active methylene group. When methylated it yields:

1-Phenyl-2:3-dimethyl-pyrazolone or **antipyrine**, $C_{11}H_{12}N_2O$, which is also produced by the action of ethyl acetoacetate upon methyl-phenyl-hydrazine, and which therefore possesses the constitutional formula (*L. Knorr*, A. **238**, 137),

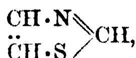


It crystallizes in small colourless plates melting at 113°. The aqueous solution is coloured red by ferric chloride and blue-green by nitrous acid. Antipyrine is an excellent febrifuge. β-Ketonic acids, β-ketonic aldehydes, β-diketones also yield pyrazole derivatives with phenyl-hydrazine.

Isomeric with pyrazole is glyoxaline (p. 561), in which the two atoms of N are separated by a C atom.

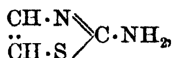
2. THIAZOLE GROUP

Thiazole,

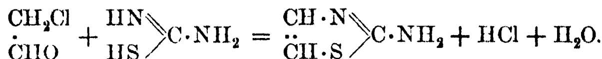


is derived from thiophene in the same way as pyridine is from benzene, by the exchange of CH for N, and closely resembles —along with its derivatives—the bases of the pyridine series in properties. It is obtained from amino-thiazole (see below) by the exchange of the amino-group for hydrogen, in a similar manner to the conversion of aniline into benzene. It is a colourless liquid, boiling at 117°, hardly distinguishable from pyridine; as a base it forms salts, but it is scarcely affected by concentrated sulphuric acid, &c. (*Hantzsch*, *Popp*, A. **250**, 273).

Amino-thiazole,



is formed by the action of mono-chloraldehyde upon thio-urea (pseudo form), thus:



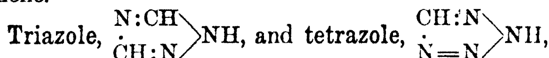
The constitution of the thiazoles follows from this and similar modes of formation. Amino-thiazole is a base of perfect "aromatic" character, like that of aniline. (Cf. *Hantzsch* and his pupils, A. **249**, 1, 7, 31; **250**, 257; **265**, 108.)

As further types of five-membered rings, may be cited:



Imidazole or glyoxalin — Oxazole,

which are related to thiazole as pyrrole and furane are to thiophene.



are examples of five-membered rings extremely rich in nitrogen. (Cf. B. **25**, 225, 1411; **26**, 2392.)

The foregoing constitutional formulæ with their double linkings correspond with *Kekulé's* benzene formula. But formulæ with centric linkings analogous to the centric benzene formula (p. 360) have been introduced. (Cf. *Bamberger*, B. **24**, 1758; A. **273**, 373; also A. **249**, 1; **262**, 265; B. **21**, Ref. 888; **24**, 3485; **27**, 3077; **28**, 1501.)

XXXVII. SIX-MEMBERED HETEROCYCLIC RINGS

Ring compounds closely related to pyrrole, thiophene, and furane, but containing six atoms in the ring (viz. five carbon atoms + one oxygen, sulphur, or nitrogen atom), are known.

The representatives of these are: **δ-valerolactone,** $CH_2{<}\begin{matrix}CH_2\cdot CH_2\\CH_2\cdot CO\end{matrix}{>}O$, **glutaric anhydride,** $CH_2{<}\begin{matrix}CH_2\cdot CO\\CH_2\cdot CO\end{matrix}{>}O$

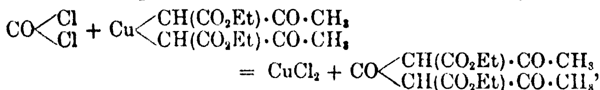
(p. 248), and more especially the **pyrones**, *e.g.* γ-pyrone, $CO<\begin{matrix}CH:CH\\CH:CH\end{matrix}>O$.

Of the nitrogen compounds, **pyridine**, $CH\begin{matrix}CH\cdot CH\\CH:CH\end{matrix}N$, and **piperidine**, $CH_2<\begin{matrix}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{matrix}>NH$, are of great importance. The derivatives of the sulphur compound, **penthiophene**, $CH_2<\begin{matrix}CH:CH\\CH:CH\end{matrix}>S$, are of but little importance.

Six-membered rings containing two nitrogen atoms are the diazines, $C_4H_4N_2$, the ortho compound is *pyridazine*, the meta *pyrimidine*, and the para *pyrazine*. The compound, $NH<\begin{matrix}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{matrix}>O$, is *morpholin*. Six-membered rings containing three and four nitrogen atoms are termed respectively triazines and tetrazines. (Cf. triazole and tetrazole, p. 564.)

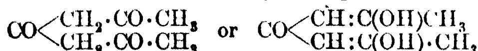
A. Pyrones

γ-**Pyrone**, a solid, m.-pt. 32·5° and b.-pt. 315°, is obtained when its dicarboxylic acid, chelidonic acid (p. 567), is heated. *αα*-**dimethyl-γ-pyrone**, $CO<\begin{matrix}CH:CMe\\CH:CMe\end{matrix}>O$, may be synthesised from cupric ethyl aceto-acetate and carbonyl chloride.



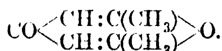
$$CO<\begin{matrix}Cl\\Cl\end{matrix} + Cu<\begin{matrix}CH(CO_2Et)\cdot CO\cdot CH_3\\CH(CO_2Et)\cdot CO\cdot CH_3\end{matrix} = CuCl_2 + CO<\begin{matrix}CH(CO_2Et)\cdot CO\cdot CH_3\\CH(CO_2Et)\cdot CO\cdot CH_3\end{matrix},$$

On hydrolysis with sulphuric acid the ester yields the free acid, which loses carbon dioxide, yielding:



$$CO<\begin{matrix}CH_2\cdot CO\cdot CH_3\\CH_2\cdot CO\cdot CH_3\end{matrix} \text{ or } CO<\begin{matrix}CH:C(OH)CH_3\\CH:C(OH)\cdot CH_3\end{matrix}$$

which immediately loses water, yielding dimethyl-γ-pyrone:



$$CO<\begin{matrix}CH:C(CH_3)\\CH:C(CH_3)\end{matrix}>O.$$

(For a modified formula, see *Collie*, J. C. S. 1904, 971.) *Collie* and *Tickle* (J. C. S. 1899, 710) have shown that this compound can form definite salts with acids, *e.g.* the hydrochloride, $C_7H_8O_2$, HCl, and oxalate. The addition of the acid undoubtedly occurs at the oxygen atom, since the salts are relatively unstable and are completely hydrolysed in dilute aqueous solution. The oxygen atom in these salts, therefore,

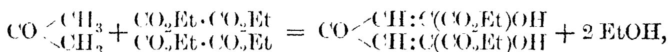
probably functionates as a tetravalent atom, $\begin{matrix}\cdot C\\ \cdot C\end{matrix}\!>O<\!\begin{matrix}H\\ Cl\end{matrix}$, and the salts are **oxonium salts** corresponding with ammonium salts.* Numerous other compounds have since been obtained, which tend to show that the oxygen atom can frequently functionate in this manner, *e.g.* numerous oxygen compounds, esters, ethers, ketones, acids, aldehydes yield definite crystalline compounds with anhydrous metallic salts, *e.g.* $MgBr_2$ or $AlCl_3$ (*Walker*, J. C. S. 1904, 1106); similar oxygen compounds also form well-defined crystalline salts with complex acids, *e.g.* ferrocyanic acid (*Baeyer* and *Villiger*, B. 1901, **34**, 2679, 3612; 1902, **35**, 1201); and even mineral acids (for summary of work, see *Knox* and *Richards*, J. C. S. 1919, **115**, 508). Since the salt is derived from a very feeble base (solutions of dimethyl-pyrone are very feeble conductors) and a relatively strong acid, the solution should be highly hydrolysed, and should give a strongly acid reaction. That the hydrolysis is not complete in the case of a moderately concentrated solution of the picrate has been shown by *Walden* (B. 1901, **34**, 4191), who compared the partition coefficient of picric acid between water and benzene both with and without the addition of dimethyl-pyrone, and found that the ratio $\frac{\text{concentration of benzene solution}}{\text{concentration of aqueous solution}}$ is less when the pyrone is present.

Other methods which have also led to the conclusion that a certain amount of salt exists in solution are (*a*) depression of the freezing-point of aqueous solutions. If no compound exists in an aqueous hydrochloric acid solution, then the depression caused would be the sum of the depressions produced by the known amounts of dimethyl-pyrone and hydrochloric acid present. The actual value obtained is less than this sum (*Walden*). (*b*) A determination of the electrical conductivity. If no compound is formed, the conductivity should be the same as that of a solution of pure hydrochloric acid of the same concentration; but if any appreciable amount of a salt is formed in solution this will give rise to a certain number of pyrylium (+) and chloride (−) ions, *i.e.* the number of hydrions will be less than in a solution of pure hydrochloric acid of the same concentration, and hence the electrical conductivity will be considerably reduced. It has actually been found that the conductivity is less, and that it tends to decrease as the solu-

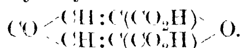
* For alternative formula for the salts see *Gibson* and *Simonsen*, J. C. S. 1928, 2307.

tion becomes more concentrated. (Cf. also *Rordam*, J. A. C. S. 1915, **37**, 557.)

γ-Pyrone-dicarboxylic acid, or chelidonic acid, occurs in the greater celandine (*Chelidonium majus*), and may be synthesised by *Claisen's* method (p. 232). Acetone and ethyl oxalate readily condense, yielding the ester of acetone-dioxalic acid or xantho-chelidonic acid:



which immediately loses water, yielding ethyl chelidonate, and this on careful hydrolysis yields chelidonic acid:



The salts of this acid are colourless, but when warmed with an excess of alkali yellow salts of xantho-chelidonic acid are formed owing to the rupture of the ring.

Pyrones with hydrogen in the presence of palladium and gum-arabic yield tetrahydro-derivatives, which boil at lower temperatures than the original substances. Pyrones in colloidal solution or as gels adsorb iodine, giving blue products, more especially 8-phenyl-γ-benzopyrone (*Barger* and *Starling*, J. C. S. 1915, **107**, 411; *A. R. Watson*, 1916, **109**, 303).

B. Pyridine

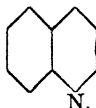
Pyridine, C_5H_5N, resembles benzene in many points:

1. It is even more stable than benzene, and does not yield substituted derivatives so readily with such reagents as sulphuric and nitric acids or the halogens. Sulphonic acids are obtained at very high temperatures only; nitro- and iodo-pyridines are as yet unknown; and only a few chloro- and bromo-pyridines have been prepared. Pyridine and its carboxylic acids are not affected by oxidizing agents.

2. Its derivatives resemble those of benzene. Thus its homologues (and also quinoline, &c.) are transformed into pyridine-carboxylic acids when oxidized, and these acids yield pyridine when distilled with lime, just as benzoic acid yields benzene.

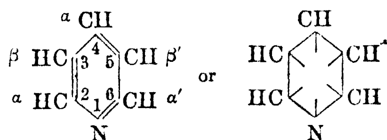
3. The isomeric relations are also precisely analogous to those of the benzene derivatives. Thus the number of the isomeric mono-derivatives of pyridine is the same as that of the isomeric bi-derivatives of benzene, viz., three; and the number of the bi-derivatives of pyridine, containing the same substituents, the same as that of the benzene derivatives C_6H_3XXX', viz., six.

4. Just as two benzene nuclei can form naphthalene, so can a benzene and a pyridine form the compound quinoline:



5. The products of reduction are likewise analogous. Pyridine like benzene yields a hexahydro-derivative, $C_5H_{11}N$, only somewhat more readily; this is known as piperidine. Quinoline yields a tetrahydro-derivative, $C_9H_{11}N$, more readily than naphthalene, and acridine readily yields a dihydro-derivative, $C_{13}H_{11}N$, which is analogous to anthracene dihydride. In these latter compounds further combination with hydrogen may take place, but there is likewise a tendency to the reproduction of the original bases.

We are therefore forced to the conclusion that pyridine has a ring constitution similar to that of benzene, and is to be represented as:



In contradistinction to the neutral benzene hydrocarbons, pyridine and its homologues are strong bases, most of them having a pungent odour; pyridine is readily soluble in water, but quinoline only slightly so. They distil or sublime without decomposition, and form salts; those with hydrochloric and sulphuric acids are for the most part readily soluble, while those with chromic acid or hydro-ferrocyanic acid, though often characteristic, are usually only sparingly soluble; they also form double salts with the chlorides of platinum, gold, and mercury, most of which are sparingly soluble, *e.g.* $(C_5H_5N)_2H_2PtCl_6$.

The bases are tertiary, and hence cannot be acetylated; they combine, however, with alkyl iodides, yielding quaternary ammonium salts, *e.g.* pyridine and methyl iodide yield C_5H_5N, CH_3I, methyl-pyridonium iodide.

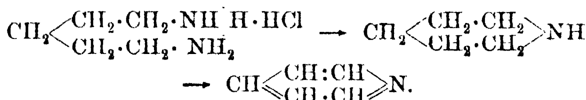
Pyridine and some of its homologues are present in coal-tar, and are therefore constituents of the lower boiling fractions. They may be extracted from these by shaking with dilute

sulphuric acid, in which they dissolve. It is also present in tobacco smoke. A number of pyridine bases are present in bone-oil or Dippel's oil, a product obtained by the dry distillation of bones from which the fat has not been extracted.

Mixtures of pyridine bases can readily be obtained from this source. Certain alkaloids (p. 592) yield pyridine or its derivatives when distilled alone or with alkalis, *e.g.* chinchonine when distilled with potash yields a dimethyl-pyridine or lutidine. Pure pyridine may be obtained by distilling its carboxylic acid with lime.

Among the more interesting methods by means of which pyridine and its derivatives have been synthesised are the following:—

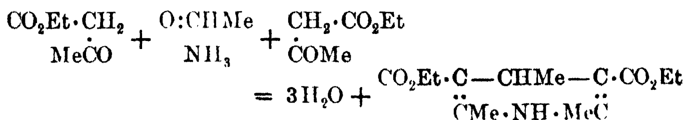
1. When pentamethylene-diamine hydrochloride is strongly heated it yields piperidine, and when this is oxidized with concentrated sulphuric acid at 300° pyridine is formed (*Ladenburg*):



A method very similar to this, which can be employed at much lower temperatures, is the elimination of hydrogen chloride from 5-chloroamylamine, $CH_2Cl\cdot(CH_2)_3\cdot CH_2\cdot NH_2$. This elimination occurs when an aqueous solution of the base is heated on the water-bath; ring formation takes place, and piperidine hydrochloride is formed (*Gabriel*). These two methods are of great importance in deciding the constitution of piperidine, and therefore indirectly that of pyridine.

2. The ammonia derivatives of various unsaturated aldehydes yield pyridine homologues when distilled (p. 137), *e.g.* β-methylpyridine is obtained from acrolein ammonia, and collidine from croton-aldehyde ammonia (*Baeyer*, A. **155**, 283, 297).

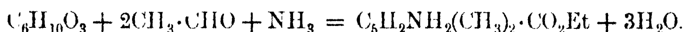
3. When ethyl acetoacetate is warmed with aldehyde-ammonia, the ester of "Dihydro-collidine-dicarboxylic acid", *i.e.* ethyl trimethyl-dihydro-pyridine-dicarboxylate is produced (*Hantzsch*) (cf. p. 238):



This loses its two "hydro"-hydrogen atoms when acted on by nitrous acid, and yields ethyl collidine-dicarboxylate, $C_5N(CH_3)_3(CO_2Et)_2$, from which collidine may be obtained by hydrolysis and elimination of carbon dioxide.

If, instead of aldehyde-ammonia, the ammonia compounds of other aldehydes are used, homologous bases of the type $C_5H_2N(CH_3)_2(C_nH_{2n+1})$ are formed.

In the above reaction a molecule of the acetoacetic ester may be replaced by one of an aldehyde, when the mono-carboxylic esters of dialkylated pyridines are formed, thus:

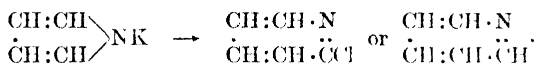


This is a very important synthetical method (*Hantzsch*, A. **215**, 1, &c.).

Two methods of obtaining pyridine derivatives, which indicate the relationship of pyridine to quinoline and pyrrole, are:

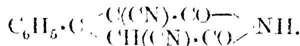
(*a*) The conversion of quinoline into quinolinic acid or pyridine $\alpha\beta$-dicarboxylic acid (p. 584).

(*b*) The conversion of potassium-pyrrole into chloro-pyridine when heated with chloroform, or into pyridine when heated with methylene-chloride:



The ring constitutional formula (p. 568) is in perfect harmony with the characteristic properties of pyridine and its derivatives, with the number of isomeric derivatives in each case, and also with the synthetical methods of formation.

4. Complex pyridine derivatives are formed by condensing ketones or aldehydes with ethyl cyanoacetate in the presence of ammonia or an amine, *e.g.* benzaldehyde gives



(G. 1918, **48**, ii, 83.)

5. Ethyl 2:6-dimethylpyridine-3:4-dicarboxylate is readily synthesised by condensing ethyl acetopyruvate, $CH_3{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}CO_2Et$, with ethyl β-aminocrotonate (p. 235) at 0° (B. 1917, **50**, 1568; 1918, **51**, 150), and from this ester the corresponding dibasic acid, and on oxidation the 2:3:4:6-tetracarboxylic acid are formed, and by elimination of carbon dioxide, 2:6-dimethylpyridine.

In order to determine the position of any given group, it is sought to exchange it for carboxyl; should picolinic acid result, the group occupies the α-position, and should nicotinic or *iso*-nicotinic, then it fills the β- or γ-position respectively, since in these acids the α-, β-, and γ-positions of the carboxyl have been determined by special means. (See M. **1**, 800; **4**, 436, 453, 595; B. **17**, 1518; **18**, 2967; **19**, 2432.)

Di-derivatives of pyridine containing the same substituent twice can exist theoretically in six isomeric forms. As a matter of fact the six dicarboxylic acids are known (αα'-, αβ-, αγ-, αβ'-, βγ-, and ββ'- (see p. 574).

The isomerism of picoline, C_6H_7N, with aniline, $C_6H_5 \cdot NH_2$, which repeats itself in their homologues, is also worthy of notice.

Pyridine, C_5H_5N (*Anderson*, 1851), may be prepared from bone-oil, and can be obtained pure by heating its carboxylic acid with lime; the ferrocyanide is especially applicable for its purification, on account of its sparing solubility in cold water. It is also found in the ammonia of commerce. Pyridine is a liquid of very characteristic odour, miscible with water, and boiling at 115°. It is used as a remedy for asthma, and also in Germany for mixing with spirit of wine in order to render the latter duty-free. When sodium is added to its hot alcoholic solution, or when solutions of its salts are electrolysed, hydrogen is taken up and piperidine, $C_5H_{11}N$, formed (*Ladenburg* and *Roth*, B. **17**, 513).

When heated strongly with hydriodic acid, pyridine is converted into normal pentane.

The ammonium iodides, *e.g.* C_5H_5N, CH_3I, give a characteristic pungent odour when heated with potash, a fact which may be made use of as a test for pyridine bases; it depends upon the formation of alkylated dihydro-pyridines, *e.g.* **dihydro-methyl-pyridine,** $C_5H_6 \cdot N(CH_3)$ (*Hofmann*, B. **14**, 1497).

Pyridine is polymerized by the action of metallic sodium to **dipyridine,** $C_{10}H_{10}N_2$ (an oil, b.-pt. 286°–290°), with the simultaneous production of *p*-**dipyridyl**, $C_5H_4N \cdot C_5H_4N$ (long needles, m.-pt. 114°), a compound corresponding to diphenyl (p. 503); both of these yield iso-nicotinic acid when oxidized. An isomeric *m*-**dipyridyl** has also been prepared, which gives nicotinic acid when oxidized.

Pyridine can be brominated but not nitrated; it can also be **sulphonated** with the formation of β-pyridine-sulphonic acid, $C_5H_4N \cdot (SO_3H)$, which with potassium cyanide yields β-**cyano-**

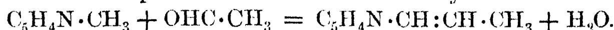
pyridine, $C_5H_4N \cdot CN$, or by fusion with potash, β-hydroxy-pyridine.

2-**Amino**- and 2:6-**diamino**-derivatives are formed by the action of sodamide on pyridine and subsequent treatment with water. They can be diazotized in the same way as aniline, and give rise to azo-dyes (Abs. 1915, i, 590).

The three **hydroxy-pyridines**, $C_5H_4N(OH)$ (α-, β-, γ-), are best prepared by the elimination of carbon dioxide from the respective hydroxy-pyridine-carboxylic acids. The melting-points are respectively: α, 107°; β, 124°; γ, 148°. They possess the character of phenols, and are coloured red or yellow by ferric chloride. As in the case of phloroglucinol, so here also there is a tertiary as well as a secondary form to be taken into account, the former reminding one of the lactams and the latter of the lactims; for instance, γ-hydroxy-pyridine may either have the "phenol" formula $C_2H_2 \lessgtr \genfrac{}{}{0pt}{}{C(OH)}{N\!=\!=} \gtrless C_2H_2$ or the "pyridone" formula $C_2H_2 \lessgtr \genfrac{}{}{0pt}{}{CO}{NH} \gtrless C_2H_2$, the latter of the two representing a keto-dihydro-pyridine. The two methyl ethers, methoxy-pyridine and methyl-pyridone, corresponding with the phenol and pyridone formulæ, are both known, and differ considerably in properties (M. **6**, 307, 320; B. **24**, 3144).

Homologues of Pyridine (cf. *Ladenburg*, A. **247**, 1).—**Methyl-pyridines** or **picolines**, $C_5H_4N(CH_3)$. All the three picolines are contained in bone-oil, and probably also in coal-tar. The β-compound is obtained from acrolein-ammonia (p. 137), and also when strychnine is heated with lime, or when trimethylene-diamine hydrochloride is distilled. They are liquids of unpleasant, piercing odour resembling that of pyridine, and they yield α-, β-, or γ-pyridine-carboxylic acid when oxidized. The boiling-points are: α, 129°; β, 142°; γ, 142°–144°. **Ethyl-pyridines**, $C_5H_4N(C_2H_5)$, are also known.

Propyl- and **isopropyl-pyridines**, $C_5H_4N(C_3H_7)$, have been carefully investigated on account of their relation to coniine. They are prepared by heating pyridine with the alkyl iodides. **Conyrine**, $C_8H_{11}N$ (liquid, b.-pt. 166°–168°), which is formed when coniine, $C_8H_{17}N$, is heated with zinc dust, and which yields coniine again when treated with hydriodic acid, is α-normal-propyl-pyridine. α-**Allyl-pyridine**, $C_5H_4N(C_3H_5)$, is formed when α-picoline is heated with aldehyde:



$$C_5H_4N \cdot CH_3 + OHC \cdot CH_3 = C_5H_4N \cdot CH{:}CH \cdot CH_3 + H_2O.$$

Reduction transforms it into inactive coniine (b.-pt. 189°–190°).

Dimethyl-pyridines or **Lutidines**, $C_5H_3N(CH_3)_2$.—The presence of three lutidines has been proved in bone-oil and coal-tar (B. **21**, 1006; **29**, 2996). *αγ*-Lutidine boils at 157°, the *αα'*-compound at 142°, and the *βγ*-compound at 164°.

The **trimethyl-pyridines** or **collidines**, $C_5H_2N(CH_3)_3$, are isomeric with the propyl-pyridines. Some of them are present in bone-oil, and can be prepared from cinchonine by distilling the latter with caustic potash (p. 600). The *s*- or *αα'γ*-collidine, obtained from the condensation product of ethyl acetoacetate and aldehyde ammonia (p. 238), or from acetamide and acetone at 250°, boils at 171°–172°. Acetophenone and benzamide yield the *s*-**triphenylpyridine** (*Pictet* and *Stehelin*, C. R. 1916, **162**, 876).

Pyridine-carboxylic Acids (*Weber*, A. 1887, **241**, 1).—The **pyridine-mono-carboxylic acids**, $C_5H_4N(CO_2H)$, are formed by the oxidation of all mono-alkyl derivatives of pyridine, *i.e.* from methyl-, propyl-, phenyl-, &c., pyridines; also from the pyridine-dicarboxylic acids by the decomposition of one of the carboxyl groups, just as benzoic may be got from phthalic acid. The carboxyl which is in closest proximity to the nitrogen is the first to be eliminated. Nicotinic acid is also produced by the oxidation of nicotine. The acids unite in themselves the characters of the basic pyridine and of an acid, and are therefore comparable with glycocoll. They yield salts with HCl, &c., and double salts with $HgCl_2$, $PtCl_4$, &c.; on the other hand, they form metallic salts as acids, those with copper being frequently made use of for the separation of the acids.

(For *constitution*, see *Skraup* and *Cobenzl*, M. 1883, **4**, 436.)

The *α*-acid is **picolinic acid**, and forms needles melting at 135°. The *β*-acid is **nicotinic acid**, and melts at 231°. The *γ*-acid is **iso-nicotinic acid**, and melts at 309° in a sealed tube. All three acids (and also the *βγ*-dicarboxylic acid) readily yield up their nitrogen as ammonia when acted upon by sodium amalgam, being thereby transformed into unsaturated acids of the fatty series (*Weidel*, M. 1890, **11**, 501).

The constitution of nicotinic acid follows from its relationship to quinoline. Quinoline on oxidation yields pyridine *αβ*-dicarboxylic acid, the constitution of which follows from the constitution of quinoline. When heated, the dibasic acid loses carbon dioxide, yielding a monobasic acid which is not identical with picolinic acid (which can be shown to be the *α*-acid), and therefore it must be pyridine *β*-carboxylic acid.

Pyridine-dicarboxylic acids, $C_5H_3N(CO_2H)_2$

α-β-	=	**Quinolinic acid**	M.-pt. 190°.
α-γ-	=	**Lutidinic acid**	M.-pt. 235°.
α-α′-	=	*Dipicolinic acid*	M.-pt. 226°.
α-β′-	=	*Iso-cinchomeronic acid*	M.-pt. 236°.
β-β′-	=	*Dinicotinic acid*	M.-pt. 323°.
β-γ-	=	*Cinchomeronic acid*	M.-pt. 266°.

Quinolinic acid, which crystallizes in short glistening prisms, is the analogue of phthalic acid, and is obtained by the oxidation of quinoline, just as phthalic acid from naphthalene; cinchomeronic and iso-cinchomeronic acids are obtained by the oxidation of cinchonine and quinine.

Hydro-pyridines.—According to theory, hexa-, tetra-, and dihydro-pyridines may exist. The first of these receive the generic name of "piperidines", *e.g.* pipecoline, $C_5H_{10}N(CH_3)$, lupetidine, $C_5H_9N(CH_3)_2$, and copellidine, $C_5H_8N(CH_3)_3$; while the tetrahydro-compounds are termed "piperideins".

Piperidine, $C_5H_{11}N$ (*Wertheim, Rochleder*, 1850), is a colourless liquid of peculiar odour, slightly resembling that of pepper, and of strongly basic properties yielding crystalline salts. It dissolves readily in water and alcohol, and boils at 106°.

It occurs in pepper in combination with piperic acid, $C_{12}H_{10}O_4$ (p. 495), in the form of the alkaloid **piperine,** $C_{17}H_{19}NO_3 = C_5H_{10}N \cdot C_{12}H_9O_3$, *i.e.* piperyl-piperidine, which crystallizes in prisms, melting at 129°; from this latter it may be prepared by boiling with alkali.

(For its formation from pyridine and from pentamethylenediamine, see pp. 203, 569, 571.)

Piperidine is a secondary amine; its imino hydrogen is replaceable by alkyl and acyl radicals. When its vapour, mixed with that of alcohol, is led over zinc dust, homologous (ethylated) piperidines are formed.

When methylated, piperidine yields, as a secondary base, in the first instance, tertiary *n*-**methyl-piperidine,** $C_5H_{10}N(CH_3)$, and then with a further quantity of methyl iodide an ammonium iodide, **dimethylpiperidonium iodide.** The corresponding hydroxide does not decompose in the usual manner when distilled, but yields water and an aliphatic base, "dimethylpiperidine", $C_7H_{15}N$ or $CH_2{:}CH \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot NMe_2$.

The latter forms a quaternary iodide, the hydroxide of which, when distilled, gives trimethylamine and piperylene, $CHMe{:}CH \cdot CH{:}CH_2$. This process of converting bases into their quaternary ammonium salts and the distillation of these

with alkalis is usually termed **exhaustive methylation**, and is largely used for preparing unsaturated compounds (cf. also chapter on Alkaloids).

The method of exhaustive methylation has also been used for ascertaining the relative stabilities of certain ring systems (*v. Braun*, B. 1916, **49**, 2629; 1922, **55**, 3818). The method is based on the use of a compound containing two different ring systems, *e.g.* pyrrolidylpiperidonium bromide,



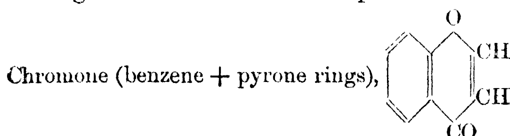
and determining which ring is ruptured under the influence of alkalis. When examined in this way piperidyl-tetrahydro-isoquinolonium hydroxide—from tetrahydro-isoquinoline, 1:5-dibromopentane and alkali—yields 1-*o*-vinylbenzyl-piperidine, $CH_2{:}CH{\cdot}C_6H_4{\cdot}CH_2{\cdot}C_5H_{10}N$, indicating that under these conditions the tetrahydro-isoquinoline ring is ruptured more readily than the piperidine ring. As the result of numerous experiments the following has been shown to be the order of increasing stability of N rings: tetrahydro-isoquinoline, dihydro-isoindole, pyrrolidine, piperidine, dihydroindole, tetrahydroquinoline.

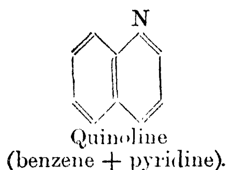
Cyanogen bromide (p. 281) can also be used for producing fission of N rings, and in this case also the order of stability is practically the same, with the exception of the dihydroindole ring $C_6H_4<\begin{matrix}CH_2\\NMe\end{matrix}>CH_2$, which, although stable when treated by the process of exhaustive methylation, is readily ruptured by cyanogen bromide (*ibid.*, 1918, **51**, 96, 255).

XXXVIII. QUINOLINE AND ACRIDINE GROUPS

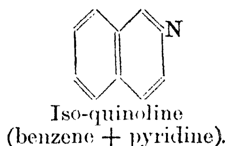
A. Quinoline Group

The quinoline group comprises the compounds formed by the condensation of a benzene nucleus with a heterocyclic six-membered ring. The best-known examples are:





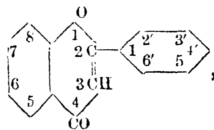
Quinoline
(benzene + pyridine).



Iso-quinoline
(benzene + pyridine).

1. CHROMONE GROUP

Chromone.—Chromone itself melts at 59° (*Ruhemann* and *Stapleton*, J. C. S. 1900, 1185), and the phenyl derivative, **flavone**, benz-2-phenyl-γ-pyrone, $C_6H_4\langle{}^{O-C \cdot C_6H_5}_{CO \cdot \ddot{C}H}$,



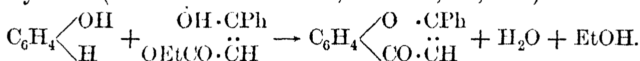
, is the parent substance of a number of yellow dyes which occur in the vegetable kingdom. The saturated analogue is termed **flavanone**, and the 3-hydroxy-flavone is termed **flavanol.**

The parent substance **chromane**, $C_6H_4\langle{}^{O\ -CH_2}_{CH_2 \cdot \dot{C}H_2}$, can be prepared (*a*) by condensing trimethylene chlorhydrin with sodium phenoxide to form phenyl *a* hydroxypropyl ether, $C_6H_5 \cdot O \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot OH$, and heating this with zinc chloride, or (*b*) by heating γ-bromopropyl phenyl ether (from trimethylene dibromide and sodium phenoxide) with zinc. Yield, 65 per cent. An attempt to prepare **chromene,** $C_6H_4\langle{}^{O-CH}_{CH_2 \cdot \ddot{C}H}$, from *o*-allylphenol by convertion into the acetate, then into the dibromide, and the action of alcoholic potash on this, gave the isomeric methylene-coumaran, $C_6H_4\langle{}^{O-}_{CH_2}\rangle C:CH_2$ (p. 554). (*Adams* and *Kindfuss*, J. A. C. S. 1919, **41**, 648). Most of the dyes are hydroxylic derivatives of flavone, and occur in nature in the form of glucosides. As examples we have **Chrysin** (dihydroxy-flavone), **Luteolin** (5:7:3′:4′-tetrahydroxy-flavone, *Kostanecki*, Abstr. 1901, **1**, 92, 335), **Quercitin** (3:5:7:3′:4′-pentahydroxy-flavone, *Herzig*, M. 1885, **6**, 872), **Myricetin** (3:5:7:3′:4′:5′-hexahydroxy-flavone), **Rhamnetin** (3:5:3′:4′-tetrahydroxy-7-methoxy-flavone), and **Rhamnazin** (3:5:4′-trihydroxy-7:3′-dimethoxy-flavone, *Perkin* and *Allison*, J. C. S. 1902, 469),

Hesperetin (5:7:3′-trihydroxy-4-methoxyflavanone, J. Pharm. S. 1927, 133).

The constitution of these compounds is often arrived at by an examination of the products formed by the action of alcoholic potash on the compound, or, more readily, by aspirating air through the dilute alkaline solution; under these conditions rhamnetin yields protocatechuic acid, 3:4-dihydroxybenzoic acid (p. 489), and phloroglucinol monomethyl ether.

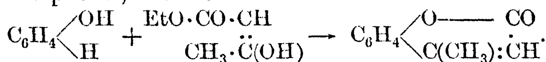
Flavone can be synthesised from phenol and the sodium derivative of ethyl benzoylacetate in the presence of phosphoric anhydride (*Simonis* and *Lehmann*, B. 1914, **47**, 692).



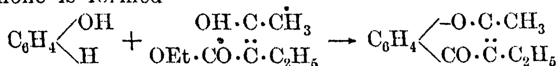
When benzoylacetonitrile (enolic form) is condensed with phenol the product is the imine corresponding with flavone, and when warmed with 20 per cent sulphuric acid the C:NH group is replaced by CO and flavone is formed (*Ghosh*, J. C. S. 1916, **109**, 105).

It can also be synthesised from β-phenoxycinnamic acid, $C_6H_5O\cdot CPh:CH\cdot CO\cdot OH$, benzene and $AlCl_3$ (*Ruhemann*, B. 1913, **46**, 2188; cf. J. A. C. S. 1919, **41**, 83), and homologues can be obtained in a similar manner.

The reaction between substituted acetoacetic esters and phenols has been closely studied. With the unsubstituted or methyl substituted ester the products are coumarin derivatives (p. 494). The ketonic esters react in their enolic forms, and the OH group of the ester reacts with the H atom ortho to the OH of the phenol, and alcohol is also eliminated.



With ethyl, phenyl, benzyl, and more complex derivatives of acetoacetic ester, the condensation proceeds in a different manner, the reactive hydrogen of the enol is eliminated with the OH group of the phenol as water, and the ring formation is completed by the elimination of EtOH and a substituted chromone is formed—



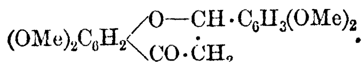
(*Jacobson* and *Ghosh*, J. C. S. 1915, **107**, 424, 959, 1051). Acetylphenyl-acetonitrile (enolic form), $OH\cdot CMe:CPh\cdot CN$, and the compounds in which Me is replaced by H or Ph,

condense more readily than the corresponding esters, and the products are γ-benzopyrones or chromones with a phenyl radical in position 3 (*Ghosh*).

A method of synthesising chromone derivatives, due to *Kostanecki* and *Tambor*, is from the condensation products of benzaldehyde, or its alkyloxy derivatives, and hydroxy-acetophenones in the presence of alcoholic potash. These products, which are termed chalkones, are hydroxyphenyl hydroxystyryl ketones and their acetyl derivatives form dibromides which react with alkalis yielding flavone derivatives. Thus $OEt \cdot C_6H_3(OH) \cdot CO \cdot CH{:}CHPh$, obtained from resacetophenone monoethyl ether, benzaldehyde, and alcoholic sodium hydroxide, yields an acetyl derivative, the dibromide of which reacts with potassium hydroxide solution yielding 7-ethoxyflavone.

m-Hydroxybenzaldehyde and resacetophenone (2:4-dihydroxyacetophenone) yield 2:4-dihydroxyphenyl 3-hydroxystyryl ketone, the triacetyl derivative of which forms a dibromide from which 7:3′-dihydroxyflavone is readily formed (*Tambor*, B. 1916, **49**, 1704; Helv. 1919, **2**, 101).

The following synthesis of quercitin is of interest (B. 1904, **37**, 1402):—2-Hydroxy-4:6-dimethoxyacetophenone and 3:4-dimethoxybenzaldehyde yield 2′-hydroxy-4′:6′:3:4-tetramethoxychalkone, $OH \cdot C_6H_2(OMe)_2 \cdot CO \cdot CH{:}CH \cdot C_6H_3(OMe)_2$, which condenses under the influence of dilute mineral acids, yielding 5:7:3′:4′-tetramethoxyflavanone,



With nitrous acid this yields the isonitroso-derivative with the $:N \cdot OH$ group in position 3, and hydrolysis converts this into the di-keto-compound $(OMe)_2C_6H_2 \left\langle \begin{matrix} O & \cdot CH \cdot C_6H_3(OMe)_2 \\ CO \cdot CO & \end{matrix} \right.$,

which readily isomerizes into $(OMe)_2C_6H_2 \left\langle \begin{matrix} O & \cdot C \cdot C_6H_3(OMe)_2 \\ CO \cdot C \cdot OH & \end{matrix} \right.$,

and this, when demethylated, yields quercitin.

When resacetophenone (2:4-dihydroxyacetophenone) is condensed with acetic anhydride and sodium acetate the product is 7-acetoxy-3-acetyl-2-methyl chromone (B. 1892, 1302). By substituting other acetophenones, *e.g.* phloracetophenone (2:4:6-trihydroxy-), gallacetophenone (2:3:4-trihydroxy-) and the

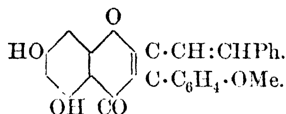
corresponding ω-methoxy-derivatives and by using the sodium salts and anhydrides of suitably substituted benzoic acids and hydrolysing the 7-acyloxy derivative, *Robinson* and his collaborators have succeeded in synthesising a large number of naturally occurring flavones. (J. C. S. 1925, 181, 1973; 1926, 2336, 2344, 2713; 1928, 1022, 3115; 1929, 61, 74, 152).

Thus resacetophenone, anisic anhydride and sodium anisate yield 7-hydroxy-4'-methoxyflavone* identical with **pratol** from Trifolium pratense. [N.B.—Using anhydrides and sodium salts of benzoic acids no acyl group is introduced in position 3.]

Galangin monomethyl ether from galanga root, 5:7-dihydroxy-3-methoxyflavone is formed from ω-methoxyphloracetophenone, benzoic anhydride and sodium benzoate. If the 3-methoxy flavones are first synthesised and then demethylated flavanols (3-hydroxyflavones) are obtained. In this way the following natural products have been synthesised:

Myricetin	(5:7:3':4':5'-pentahydroxy-flavanol).
Datiscetin	(5:7:2'-trihydroxy-).
Kaempferol	(5:7:4'-trihydroxy-).
Fisetin	(7:3':4'-trihydroxy-).
Quercitin	(5:7:3':4':-tetrahydroxy-).
Morin	(5:7:2':4'-tetrahydroxy-).
Gossypetin	(5:7:8:3':4'-pentahydroxy-).
Quercetagetin	(5:6:7:3':4'-pentahydroxy-).

It has been found possible to synthesise *iso*-flavone, or 3-phenylchromone, derivatives by somewhat similar methods, *e.g.* **genista**, 5:7:4'-trihydroxy-3-phenylchromone, the product from *Genista tinctora.* This method consists in employing a ketone like 2:4:6-trihydroxyphenyl *p*-methoxybenzyl ketone with cinnamic anhydride and sodium cinnamate, the product,



when completely methylated and oxidized gives the 2-carboxylic acid, this when heated loses carbon dioxide and on demethylation gives genista.

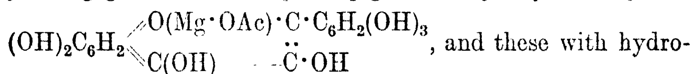
For other *iso*-flavone derivatives cf. J. C. S. 1928, 1022, 1929, 152, 1468, 1593.

On dehydrating catechin tetra-methyl ether, 5:7:3':4'-tetra-

* For numbering, cf. p. 576.

methoxy-2:3-dihydroflavanol a change of the 3:4-dimethoxyphenyl group from position 2 to 3 occurs, so that the resulting product is 5:7:3′:4′-tetramethoxy*iso*flavone (*Freudenberg*, A. 1925, **441**, 157; **446**, 87.

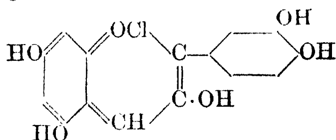
Diflavone derivatives have been recently prepared. They are derived from dichromone—the condensation product of two pyrone and one benzene ring—



Cf. *Ryan* and *O'Neill*, Abs. 1915, i, 707, 1071; 1916, i, 662, 663.

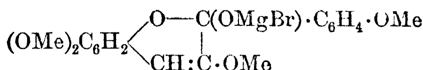
Hydroxy flavones react with magnesium and acetic acid, yielding green or bluish-green pigments, *e.g.* myricetin yields $(OH)_2C_6H_2\langle^{O(Mg\cdot OAc)\cdot C\cdot C_6H_2(OH)_3}_{C(OH)\cdots\cdots C\cdot OH}$, and these with hydrochloric acid yield red pigments containing Cl in place of Mg·OAc (J. A. C. S. 1919, **41**, 208).

Cyanidin chloride, $C_{15}H_{11}O_6Cl$, and similar products, **anthocyanidins,** obtained by hydrolysing the glucosidic plant pigments, anthocyanins (Chap. XLII, B.), are related to the flavone dyes (*Willstätter*, Abs. 1914, i, 564, 1081), as proved by the formation of phloroglucinol and hydroxybenzoic acids with alkalis at high temperatures, thus pelargonidin yields *p*-hydroxybenzoic acid, cyanidin yields protocatechuic acid, and delphinidin gallic acid. For **cyanidin chloride** the formula



has been deduced from the fact that quercitin, 3:5:7:3′:4′-pentahydroxyflavone, is reduced at 35° in alcoholic solution by magnesium and hydrochloric acid in the presence of mercury to a mixture of cyanidin and *allo*-cyanidin chlorides. In this reaction the CO group is reduced to CH·OH and HCl adds on to the pyrone O atom, and finally water is eliminated from the OH of the CH·OH group and the H attached to the para O atom. **Pelargonidin** has a similar structure, but with no OH group in position 3′, and **delphinidin chloride** has an extra OH in position 5′. The corresponding compounds from the bilberry and grape are termed **myrtillidin chloride** and **oenidin chloride,** and are the 7-monomethyl

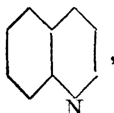
and 3:4′-dimethyl ethers of delphinidin chloride. (B. 1914, **47,** 2831; A. 1915, **408,** 1; 1916, **412,** 113.) These salts are more stable than the oxonium salts of pyrones (p. 566), but undergo appreciable hydrolysis, probably accompanied by isomerization in dilute aqueous solution as colourless products are formed. (Compare *Everest*, P. R. S. 1914, **87 B,** 444.) Pelargonidin has been synthesised by the following process:—3:5:7-trimethoxy-coumarin as a ketone reacts with the magnesium derivative of *p*-bromoanisole, $BrMg{\cdot}C_6H_4{\cdot}OMe$, yielding the additive compound,



and this with HCl gives the chloride containing Cl in place of OMgBr, and by hydrolysing the OMe groups with hydriodic acid the corresponding hydroxy compound is formed. For later syntheses cf. *Robertson*, *Robinson*, and *Struthers*, J. C. S. 1928, 1455.

2. QUINOLINE AND ITS DERIVATIVES

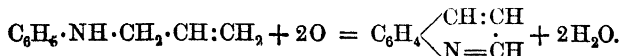
Quinoline,



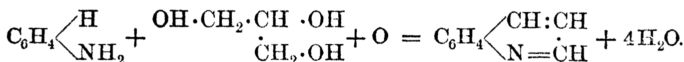
bears the same relationship to naphthalene that pyridine does to benzene, its molecule consisting of condensed benzene and pyridine nuclei. It occurs, together with derivatives, in both coal-tar and bone-oil, and may be obtained by heating certain alkaloids with potash, *e.g.* cinchonine yields quinoline itself (*Gerhardt*, 1842), and quinine gives methoxy-quinoline.

Among the various syntheses of quinoline and its derivatives the following may be noted:—

1. The first synthesis (*Koenigs*) was by the oxidation of allyl-aniline by passing its vapour over heated lead oxide:

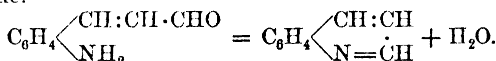


2. In the common synthesis (*Skraup*, B. **14**, 1002) aniline is heated with glycerol and sulphuric acid in presence of nitrobenzene or arsenic acid as oxidizing agent:

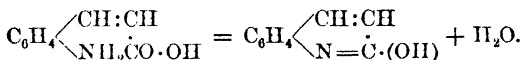


The intermediate products are probably acroleïn and acroleïn-aniline, $C_6H_5 \cdot N:CH \cdot CH:CH_2$. The homologues and analogues of aniline yield homologues and analogues of quinoline by corresponding reactions; when a naphthylamine is used, the more complicated naphtho-quinolines are formed.

3. *Baeyer* and *Drewson* (B. **16**, 2207) obtained quinoline by the elimination of the elements of water from *o*-amino-cinnamic aldehyde:

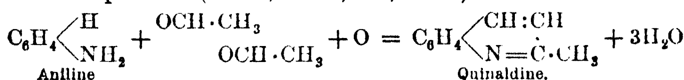


If *o*-amino-cinnamic acid is used, carbostyril (α-hydroxyquinoline, p. 585) is obtained (*Baeyer*):



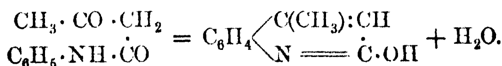
4. When aniline is heated with aldehyde (paraldehyde) and hydrochloric acid, α-methyl-quinoline (quinaldine) is obtained (*Doebner* and *v. Miller*).

In this reaction ethylidene-aniline is formed as an intermediate product (B. **24**, 1720; **25**, 2072):

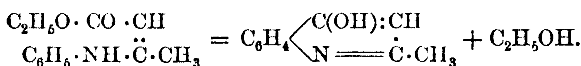


Here, again, various other primary arylamines may be used instead of aniline, and other aldehydes (B. **18**, 3361) or ketones (*e.g.* B. **19**, 1394) instead of paraldehyde.

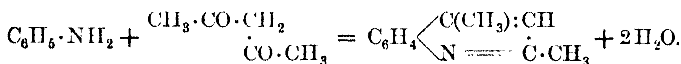
5. Aniline and acetoacetic acid combine together at temperatures above 110° to aceto-acetanilide, $CH_3 \cdot CO \cdot CH_2 \cdot CO \cdot NH \cdot C_6H_5$, from which γ-methyl-α-hydroxy-quinoline ("methylcarbostyril" is formed by the elimination of water (*Knorr*, A. 1886, **236**, 75):



Aniline can also react with acetoacetic ester below 100°, yielding **ethyl β-phenyl-amino-crotonate,** $C_6H_5 \cdot NH \cdot C(CH_3):CH \cdot CO_2C_2H_5$, which yields γ-hydroxy-quinaldine when heated (*Conrad* and *Limpach*, B. **20**, 944):

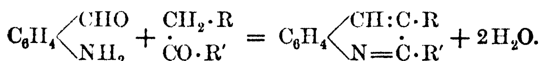


β-Diketones and other compounds closely related to acetoacetic ester also condense with aniline. In place of β-diketones, mixtures of ketones and aldehydes, or mixtures of aldehydes which would yield β-diketones or β-ketonic aldehydes if condensed together (*C. Beyer*, B. **20**, 1767), can be employed. With acetyl-acetone we obtain αγ-dimethyl-quinoline (B. 1899, **32**, 3228):



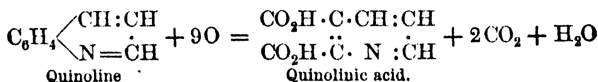
These reactions are nearly allied to those already spoken of under 4.

6. *o*-Amino-benzaldehyde condenses with aldehydes and ketones under the influence of dilute caustic soda solution, yielding quinoline derivatives (*Friedländer*, B. **15**, 2574; **16**, 1833; **25**, 1752.) With aldehyde quinoline itself results, and with acetone quinaldine:

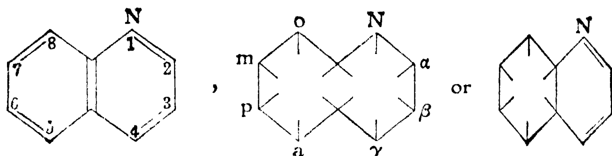


Acetophenone, acetoacetic ester, malonic ester, diketones, &c., also react in a similar way.

Constitution.—The above modes of formation (especially 3 and 6) show that quinoline is an ortho-di-substituted-derivative of benzene, and that it contains its nitrogen linked directly to the benzene nucleus; they also show that the three carbon atoms, which enter the complex, form a new hexagon (*pyridine*) ring with this nitrogen and with two carbon atoms of the benzene ring. The latter point also follows from the oxidation of quinoline to pyridine-dicarboxylic acid (*Hoogewerff* and *van Dorp*):

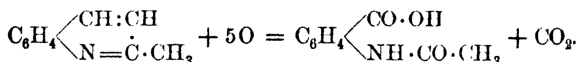


We have thus the following constitutional formula:



according to which quinoline is constituted in a manner perfectly analogous to naphthalene, and may be regarded as derived from the latter by the exchange of CH for N, or as formed by the "condensation" of a pyridine and a benzene nucleus.

When quinoline derivatives are oxidized, the benzene ring is usually more readily ruptured than the pyridine one, *e.g.* quinoline yields pyridine-dicarboxylic acid (p. 574). α-Methyl-quinoline gives, on the other hand, *o*-acetyl-amino-benzoic acid when oxidized:



$$C_6H_4\langle{}^{CH:CH}_{N=\dot{C}\cdot CH_3} + 5O = C_6H_4\langle{}^{CO\cdot OH}_{NH\cdot CO\cdot CH_3} + CO_2.$$

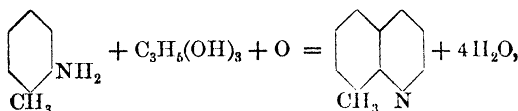
(For laws governing the oxidation of quinoline derivatives, see *W. v. Miller*, B. **23**, 2252, **24**, 1900; M. 1891, **12**, 304.)

The pyridine nucleus of quinoline takes up hydrogen more readily than the benzene one; thus quinoline is easily converted, even by tin and hydrochloric acid, into tetrahydroquinoline. It can be further reduced to the deca-hydride, but only with difficulty (B. 1922, 3779.)

The three hydrogen atoms of the pyridine nucleus, counting from the N, are designated as α-, β-, and γ-, and the four hydrogen atoms of the benzene nucleus as *o*-, *m*-, *p*-, and *a*- (ana-) hydrogen atoms, or more commonly the numbering shown above is adopted, the nitrogen atom being numbered 1 and the carbon atoms consecutively 2, 3, &c., up to 8. As no two hydrogen atoms are symmetrically situated in the molecule, seven mono-substituted derivatives of quinoline are in each case theoretically possible. As a matter of fact, all seven quinoline-monocarboxylic acids have been prepared.

The position of the substituents follows: (*a*) from the nature of the oxidation products, *e.g.* B-quinoline-carboxylic acid (*i.e.* an acid in which the carboxyl is attached to the benzene nucleus) yield a pyridine-dicarboxylic acid, while a Py-quino-

line-carboxylic acid (in which the carboxyl is linked to the pyridine nucleus) yields a pyridine-tricarboxylic acid; (*b*) from the synthesis of the compound in question. The methyl-quinoline, for instance, which is obtained from *o*-toluidine by the *Skraup* synthesis must be the 8-methyl-quinoline:



whilst *m*-toluidine must yield a 7- or 5-, and *p*-toluidine a 6-methyl-quinoline.

Quinoline (*Runge*, 1834) is a colourless strongly refracting liquid of a peculiar and very characteristic odour. It boils at 239°, is a mono-acid base, forms a sparingly soluble dichromate, $(C_7H_9N)_2, H_2Cr_2O_7$, and is used as an antifebrile. As a tertiary base it yields **quinolonium** salts (*Roser*, A. 1893, **272**, 221).

Nascent hydrogen transforms it first into **dihydro-quinoline**, C_9H_9N, which melts at 161°, and then into **tetrahydro-quinoline**, $C_9H_{11}N$, $C_6H_4\left\langle\begin{matrix}CH_2\cdot CH_2\\ NH\cdot CH_2\end{matrix}\right.$, a liquid boiling at 245°. Since both of these yield nitrosamines and can be alkylated, they are secondary bases. The tetrahydro-compound exerts a stronger antifebrile action than the mother substance, especially in the form of its ethyl derivative, **cairolin** (B. **16**, 739).

Quinoline decahydride, $C_{10}H_{17}N$, is obtained when strong reducing agents are employed. It forms crystals of a narcotic, coniine-like odour, melts at 48°, and boils at 204°.

Halogen derivatives of quinoline and nitro-quinolines have been prepared by the *Skraup* reaction, &c.; and, from the reduction of the latter, amino-quinolines, $C\ H_6N(NH_2)$. The quinoline-sulphonic acids yield cyano-quinolines with potassium cyanide, and hydroxy-quinolines when fused with potash.

1-Hydroxy-quinoline, *carbostyril*, is a quinoline hydroxylated in the pyridine nucleus (see p. 582, mode of formation 3). It crystallizes in colourless needles, melts at 198°, and is soluble in alkali, from which it is again thrown down by carbonic acid. Its constitution follows from its formation from *o*-amino-cinnamic acid (p. 486).

Quinaldine, 2-*methyl-quinoline*, $C_{10}H_9N$, is contained in coal-tar. It is a colourless liquid of quinoline odour, and boils at

246°. When oxidized with chromic acid it yields a quinoline derivative, with permanganate a pyridine-tricarboxylic acid.

The hydrogen of the methyl group readily enters into reaction; quinaldine condenses with phthalic anhydride to produce the dye, **quinoline-yellow,** $C_{10}H_7N(CO)_2C_6H_4$, the disulphonic acid of which is **quinoline-yellow S.** A mixture of quinoline and quinaldine is transformed into the (unstable) blue dyes, the **cyanines,** when alkylated and treated with caustic potash. These are used as sensitizers for photographic plates.

Quinoline-carboxylic Acids.—Cinchoninic acid, *quinoline*-4-*carboxylic acid*, $C_9H_6N(CO_2H)$, which is obtained by the oxidation of cinchonine with permanganate of potash, crystallizes in needles or prisms and melts at 254°. From it is derived **quinic acid,** 6-*methoxy-quinoline*-4-*carboxylic acid*, $C_9H_5N(OCH_3)\cdot CO_2H$, which is obtained by oxidizing quinine with chromic acid; it forms yellow prisms, melting at 280°. **Quinoline-2:3-dicarboxylic acid,** or *acridinic acid,* is formed by the oxidation of acridine.

3. ISO-QUINOLINE

Iso-quinoline, an isomer of quinoline, occurs along with the latter in coal-tar (B. **18**, Ref. 384). It is a solid, melts at 23°, and boils at 240°. Since oxidation converts it into cinchomeronic acid on the one hand and phthalic acid on the other it possesses the constitution:



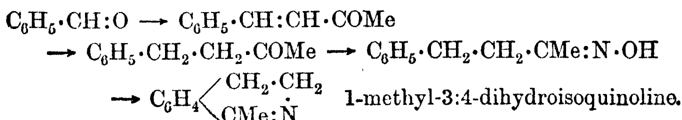
$$C_6H_4\left\langle\begin{matrix}CH:N\\ \vdots\\ CH:CH.\end{matrix}\right.$$

Its constitution also follows from its synthesis* from homophthalic acid, $C_6H_4\left\langle\begin{matrix}CH_2\cdot CO_2H\\ CO_2H\end{matrix}\right.$, in which the substituents are in the *o*-position. This may be converted into its imide, $C_6H_4\left\langle\begin{matrix}CH_2\cdot CO\\ \vdots\\ CO—NH\end{matrix}\right.$, by heating the ammonium salt. This imide with phosphorus oxychloride reacts as the tautomeride, $C_6H_4\left\langle\begin{matrix}CH = C(OH)\\ \vdots\\ C(OH):N\end{matrix}\right.$, and yields the corresponding dichloro-

*For synthesis from β-naphthaquinone see B, **25**, 1138, 1493; **27**, 198 and for synthesis from benzylaminoacetaldehyde hydrochloride and sulphuric acid see *E. Fischer*, B, **26**, 764.

iso-quinoline, which is reduced by hydriodic acid and red phosphorus to iso-quinoline.

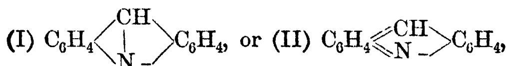
A simple synthesis of iso-quinoline derivatives is as follows:—An unsaturated ketone is formed by condensing an aromatic aldehyde with acetone; this is reduced and then converted into the oxime, from which by the *Beckmann* rearrangement dihydroisoquinolines are formed together with other products (B. 1916, **49**, 675):



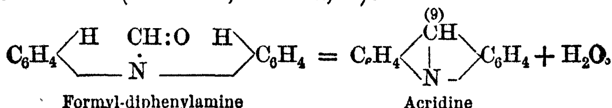
B. The Acridine Group

Acridine, $C_{13}H_9N$ (*Graebe* and *Caro*), is a basic constituent of the crude anthracene of coal-tar, and also of crude diphenylamine. It crystallizes in colourless needles, may be sublimed, and is characterized by an intensely irritating action upon the epidermis and the mucous membrane, and also by the greenish-blue fluorescence shown by dilute solutions of its salts.

Acridine stands in the same relationship to anthracene that pyridine does to benzene or quinoline to naphthalene. It may be regarded as anthracene in which one of the CH groups of the middle ring is replaced by N. The constitutional formula:

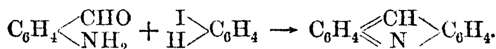


is based (*a*) upon the oxidation of acridine to quinoline-2:3-dicarboxylic acid, and to pyridine tetracarboxylic acid—the *p*-union between C and N in I becomes ruptured during the oxidation; (*b*) upon its synthesis from diphenylamine and formic acid, or formyl-diphenylamine, $(C_6H_5)_2N{\cdot}CHO$, with zinc chloride (*Bernthsen*, A. **224**, 1):



Formyl-diphenylamine   Acridine

It is also obtained when the vapour of *o*-tolyl-aniline is passed through a red-hot tube. An interesting synthesis is by boiling *o*-aminobenzaldehyde and iodobenzene in nitrobenzene solution with Na_2CO_3 and Cu powder (B. 1917, **50**, 1306):

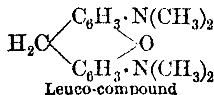


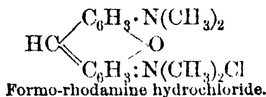
Acridine is a tertiary base, and as such combines with alkyl iodides, yielding **acridonium iodides.** It is a much feebler base than quinoline, and on reduction readily forms a dihydro-derivative, which is not basic.

9-Methyl- and **butyl-acridines, phenyl-acridine,** and **naphtho-acridines** (*i.e.* acridines which contain $C_{10}H_6$ instead of C_6H_4) have all been prepared synthetically.

Acridine, like anthracene, is a chromogene, and gives rise to the acridine dyes (Chap. LV, F.).

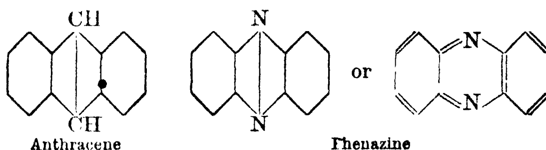
The oxygen analogue of dihydro-acridine, $C_6H_4<\genfrac{}{}{0pt}{}{CH_2}{NH}>C_6H_4$, is **diphenylene-methane oxide,** or **xanthene,** $C_6H_4<\genfrac{}{}{0pt}{}{CH_2}{-O-}>C_6H_4$, a decomposition product of aluminium phenoxide, also obtained by distilling euxanthone over zinc dust. It crystallizes in plates, and melts at 98·5°. It is on the one hand the mother substance of **xanthone,** $C_6H_4<\genfrac{}{}{0pt}{}{CO}{-O-}>C_6H_4$, and its derivative **euxanthone** or *dihydroxy-xanthone,* $OH\cdot C_6H_3<\genfrac{}{}{0pt}{}{CO}{-O-}>C_6H_3\cdot OH$, and, on the other hand, of the rhodamines and fluoresceins (p. 525). Its **tetramethyl-diamino)** derivative results from the condensation of formaldehyde with *m*-dimethylamino-phenol to tetramethyl-diamino-dihydroxy-diphenyl-methane and subsequent elimination of water (ring formation), and is the leuco-compound of **formo-rhodamine** or *pyronine*, $C_{17}H_{19}N_2OCl$, into which it passes upon oxidation and production of quinoid linking, thus:


Leuco-compound


Formo-rhodamine hydrochloride.

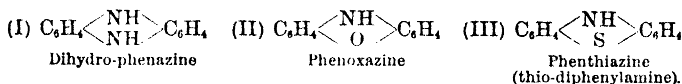
XXXIX. SIX-MEMBERED HETEROCYCLIC COMPOUNDS WITH NOT MORE THAN FOUR CARBON ATOMS IN RING. AZINES, ETC.

A number of six-membered heterocyclic compounds, containing four carbon and two other atoms, are known, *e.g.* **paroxazine,** with 4C, 1O, and 1N, the O and N in the *p*-position. A derivative of this is **morpholine,** $O<^{CH_2\cdot CH_2}_{CH_2\cdot CH_2}>NH$. Similarly, **thiazines** (4C, 1S, 1N) and **diazines** (4C, 2N) are known; and these are the parent substances of numerous important dyes. The majority of these dyes are not simple derivatives of oxazines, thiazines, or diazines, but are derived from condensed benzene and oxazine, or benzene and diazene nuclei, and may be compared with anthracene. For example, **phenazine** is anthracene in which two CH-groups have been replaced by two N-radicals:



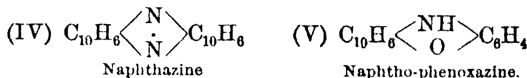
Anthracene Phenazine

dihydro-phenazine corresponds with dihydro-anthracene, and phenoxazine with dihydro-anthracene in which one CH_2 has been replaced by O and another by NH, *e.g.*:



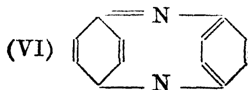
Dihydro-phenazine Phenoxazine Phenthiazine (thio-diphenylamine).

Further, the benzene nuclei may be replaced by those of naphthalene, with the formation of:



Naphthazine Naphtho-phenoxazine.

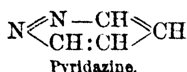
An isomeride obtained from *p*-chloraniline, $ZnCl_2$ and $AlCl_3$, is represented by formula VI, and contains a ring with 10 atoms.



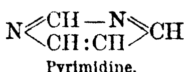
The compounds (I–III) of the type of dihydro-anthracene are the leuco-compounds of dyes when they contain an amino- (alkylamino-) or hydroxy-group in the *para*-position to the nitrogen. The dyes themselves are derived from amino- or hydroxy-phenazines (see Chap. LV, H.).

THE DIAZINES

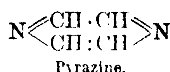
The three simple diazines are:



Pyridazine.



Pyrimidine.



Pyrazine.

Pyridazine is a colourless liquid, b.-pt. 208°, is miscible with water, has an odour of pyridine, and forms soluble salts. (Preparation, B. **28,** 451; Derivatives, Annales, 1914, ix. **2,** 403.)

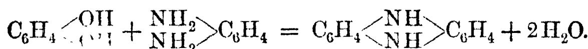
Pyrimidine can be obtained from barbituric acid and from methyluracil (p. 297); it forms colourless crystals, m.-pt. 22° and b.-pt. 124°. The pyrimidine ring is met with in uric acid and in most purine derivatives (cf. B. **34**, 3248).

Pyrazine forms colourless prisms, m.-pt. 47°, b.-pt. 118°, and is basic (J. pr. [ii], **51,** 449). **Dimethylpyrazine,** *Ketin*, is present in crude amyl alcohol, and can be obtained by the reduction of isonitrosoacetone or by condensation of amino-acetone. **Tetraphenylpyrazine** is readily obtained from benzoin. Hexahydropyrazine or **piperazine** is diethylene-diamine and is a solid, m.-pt. 104°, b.-pt. 145°, and is used in medicine as a uric acid eliminant. It is manufactured by the action of ethylene bromide on aniline, converting the diphenyldiethylene-diamine $C_6H_5{\cdot}N<\substack{C_2H_4\\C_2H_4}>NC_6H_5$ into its di-*p*-nitroso-derivative and hydrolysing this to phenol and piperazine.

Of the compounds formed by the union of a benzene and a diazine nucleus the most important is **quinoxaline,** $C_6H_4<\substack{N:CH\\ \vert \\ N:CH}$, which is obtained from *o*-phenylene-diamine and glyoxal. Substituted quinoxalines are formed by condensing *a*-diketones, *a*-ketonic acids, &c., with *o*-phenylene-diamines. Of more importance is the group of compounds containing two benzene nuclei condensed with one diazine ring, *e.g.* phenazine.

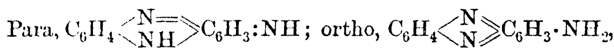
Phenazine, or *azo-phenylene* (p. 589), is obtained by the distillation of barium azo-benzoate, or by leading the vapour of

aniline through red-hot tubes; also from nitrobenzene, aniline, and sodium hydroxide at 140°, or by the oxidation of its hydro-compound (see below). It crystallizes in beautiful, long, bright-yellow needles melting at 171°, and can be readily sublimed. It is only sparingly soluble in alcohol, but readily in ether, and also dissolves in concentrated sulphuric acid to a red solution; the alcoholic solution yields a green precipitate on the addition of stannous chloride. When reduced with ammonium sulphide it yields the colourless hydro-compound, **dihydro-phenazine,** $C_{12}H_{10}O_2$, which may be obtained synthetically by heating catechol with *o*-phenylene-diamine:



$$C_6H_4<\begin{matrix}OH\\OH\end{matrix} + \begin{matrix}NH_2\\NH_2\end{matrix}>C_6H_4 = C_6H_4<\begin{matrix}NH\\NH\end{matrix}>C_6H_4 + 2H_2O.$$

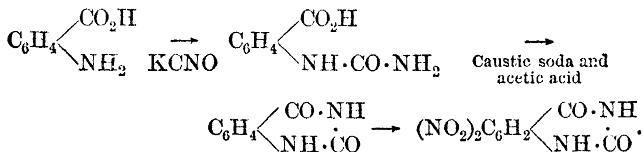
The entrance of hydroxy- or amino-groups into these azines converts them into dyes. In accordance with modern views of the quinonoid structure of dyes these derivatives are usually given ortho or para quinonoid formulæ:



$$\text{Para, } C_6H_4<\begin{matrix}N=\\NH\end{matrix}>C_6H_3{:}NH\text{; ortho, } C_6H_4<\begin{matrix}N\\N\end{matrix}>C_6H_3\cdot NH_2,$$

and similarly for hydroxy derivatives. For the more important of these dyes cf. Chap. LV, H.

An indicator, $(NO_2)_2C_6H_2<\begin{matrix}CO\cdot NH\\NH\cdot CO\end{matrix}$, a pyrimidine derivative, can be obtained from anthranilic acid by the following series of reactions:



$$C_6H_4<\begin{matrix}CO_2H\\NH_2\end{matrix} \xrightarrow{KCNO} C_6H_4<\begin{matrix}CO_2H\\NH\cdot CO\cdot NH_2\end{matrix} \xrightarrow{\text{Caustic soda and acetic acid}}$$

$$C_6H_4<\begin{matrix}CO\cdot NH\\NH\cdot CO\end{matrix} \rightarrow (NO_2)_2C_6H_2<\begin{matrix}CO\cdot NH\\NH\cdot CO\end{matrix}.$$

It gives a greenish-yellow colour with hydrion concentrations of 10^{-8}; below 10^{-6} it is colourless (J. A. C. S. 1916, **38,** 1606).

PHENOXAZINES AND PHENTHIAZINES

Phenoxazine (p. 589) is obtained by heating catechol with *o*-aminophenol, and crystallizes in plates. The leuco-compound of *nile blue* is a diethyldiamino-naphthaphenoxazin. For phenoxazine dyes see Chap. LV, H.

XL. ALKALOIDS

The group of alkaloids at one time comprised the whole of the nitrogenous basic compounds present in plants or derived from the various plant tissues by distillation. Thus methylamine, betaïne, asparagine, caffeine, and the opium alkaloids were all grouped together; but as their constitutional formulæ were established they were grouped with the compounds to which they were closely related, *e.g.* methylamine with the primary aliphatic amines, betaïne with the alkyl derivatives of glycocoll, and caffeine with the uric acid or purine derivatives. The name is now largely restricted to the nitrogenous basic plant constituents which can be regarded as derived from pyridine, quinoline, or iso-quinoline, and to those of unknown constitution.

They form an extremely important group of compounds on account of their physiological properties, and they constitute the active principles of the common vegetable drugs and poisons.

With a single exception they occur exclusively in dicotyledons, and as a rule do not exist in the free state, but combined with organic acids in the form of salts. Such acids are malic (p. 256), citric (p. 271), and tannic (p. 490); quinic acid usually accompanies the alkaloids of opium.

A few of the alkaloids are built up of carbon, hydrogen, and nitrogen, *e.g.* coniine, nicotine. Such compounds as a rule are liquids and are readily volatile; the majority, on the other hand, contain in addition oxygen, and then are usually crystalline and non-volatile. All are optically active, and as a rule lævo-rotatory. A few like coniine are secondary bases, but the majority are tertiary, and a few quaternary ammonium compounds.

The following reagents as a rule precipitate the alkaloids in the form of complex derivatives from solutions of their salts, viz. tannin, phosphomolybdic acid, a potassium iodide solution of iodine, and also potassium mercuric iodide. They are further characterized by their bitter astringent taste and by their poisonous properties. Each individual alkaloid gives characteristic colour reactions.

The alkaloids are usually extracted from plant tissues by lixiviating the finely-divided tissue with acidified water. The

extract is then rendered alkaline with ammonia and the free alkaloid separated by filtration, or, if it is at all readily soluble, by extraction with chloroform.

Among the reactions made use of in elucidating the structure are:—

1. Determination of the number of free hydroxyl groups by acetylation (cf. p. 209). Thus morphine can be shown to contain two, codeine one, and papaverine none.

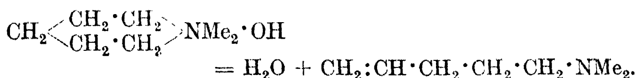
2. Determination of methoxy, OMe, groups by *Zeisel's* method or *Perkin's* modification. Determination of NMe, methylimino, groups by heating the hydriodide at 300° and estimating the CH_3I eliminated (*Herzig* and *Meyer*).

3. Study of the action of hydrolysing agents. Esters are hydrolysed, but most other types of linking are resistent to such agents. Narcotine (p. 601) yields opianic acid and hydrocotarnine, and is presumably an ester derived from these two compounds. Similarly, atropine (p. 607) on hydrolysis yields tropic acid and tropine. As the products of hydrolysis are simpler than the original alkaloid, the elucidation of their constitutions is less difficult.

4. Examination of the products of oxidation. Thus codeine contains a secondary alcoholic group, as on oxidation it yields a ketone, codeinone, containing the same number of carbon atoms. Coniine when oxidized yields picolinic acid, and must thus be an α-substituted derivative of pyridine. Cinchonine yields quinoline-γ-carboxylic acid.

5. Determination of the primary, secondary, tertiary, or quaternary nature of the base.

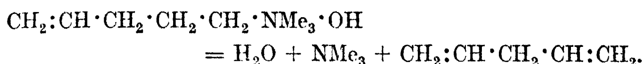
6. Study of the degradation products obtained by exhaustive methylation. As an example of this method the simple secondary amine piperidine may be taken. When methylated by means of methyl iodide it yields first the tertiary amine methylpiperidine, and finally the quaternary ammonium iodide dimethylpiperidonium iodide. This with moist silver oxide yields the quaternary base, which on distillation decomposes into water and an unsaturated aliphatic tertiary amine:



$$CH_2{<}\begin{matrix}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{matrix}{>}NMe_2\cdot OH = H_2O + CH_2{:}CH\cdot CH_2\cdot CH_2\cdot CH_2\cdot NMe_2.$$

When methylated and treated with silver oxide this unsaturated base yields a quaternary hydroxide, which splits

up into water, trimethylamine, and $\Delta^{\alpha\delta}$ pentadiene when distilled:

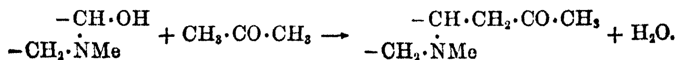


$$CH_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}NMe_3{\cdot}OH = H_2O + NMe_3 + CH_2{:}CH{\cdot}CH_2{\cdot}CH{:}CH_2.$$

7. An examination of the products obtained by fusing the alkaloid with potash or by distilling it with zinc dust. Thus morphine and zinc dust yield phenanthrene together with other products, and hence the molecule of morphine probably contains a phenanthrene ring. Papaverine, when fused with potash, yields dimethoxy-iso-quinoline and 3:4-dimethoxy-toluene, and hence papaverine is probably an iso-quinoline derivative. The processes of fusion with potash and distillation with zinc dust require high temperatures, and as molecular rearrangements occur much more readily at high than at low temperatures, the conclusions drawn from a study of the products formed during such processes should be accepted with a certain amount of reserve unless supported by other evidence.

The alkaloids can be grouped according to their origin, *e.g.* the opium alkaloids, bases from solanine, &c., or according to the heterocyclic ring which they contain. The latter method is adopted here, and we thus have the pyridine, quinoline, *iso*-quinoline, and phenanthrene groups.

Many of the alkaloids are extremely complex, and several, *e.g.* quinine and strychnine, have so far not been synthesised in the laboratory. The function of such complex nitrogenous compound in the plant system and the manner in which the complexes are built up in the tissue are problems which have aroused much interest. *Robinson* in "A Theory of the Mechanism of the Phytochemical Synthesis of certain Alkaloids" (J. C. S. 1917, **111,** 876) has suggested probable methods of formation. The two main reactions which bring about union between carbon and carbon are (1) the aldol condensation (p. 138) of aldehydes, and (2) the condensation of an aldehyde or ketone with ammonia or an amine to a carbinol-amine, $> C(OH){\cdot}N <$, and the reaction of this with substances containing the group, $> CH{\cdot}CO —$, *e.g.*:

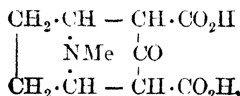


$$\begin{matrix}-CH{\cdot}OH \\ -CH_2{\cdot}\dot{N}Me\end{matrix} + CH_3{\cdot}CO{\cdot}CH_3 \longrightarrow \begin{matrix}-CH{\cdot}CH_2{\cdot}CO{\cdot}CH_3 \\ -CH_2{\cdot}\dot{N}Me\end{matrix} + H_2O.$$

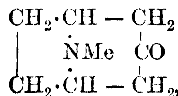
Reactions of this type require no condensing agent, and proceed almost to completion in aqueous solution at the ordinary temperature. The important starting-points are ammonia, formaldehyde, ornithine (arginine), and lysine (pp. 227 and 654), and degradation products of carbohydrates, more particularly citric acid, which can give rise to acetonedicarboxylic acid on oxidation, and this supplies the acetone complex.

Thus lysine, $NH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH(NH_2) \cdot CO_2H$, with formaldehyde undergoes methylation and oxidation, giving $NHMe \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CH{:}O$, which with more formaldehyde produces $NMe\left\langle\begin{matrix} CH_2 \text{———} CH_2 \\ CH(OH) \cdot CH_2 \end{matrix}\right\rangle CH_2$, and this with acetone yields $NMe\left\langle\begin{matrix} CH_2 \text{—————} CH_2 \\ CH(CH_2 \cdot COMe) \cdot CH_2 \end{matrix}\right\rangle CH_2$, the alkaloid methyl-pelletierine of the pomegranate trees.

Similarly, tropinone (p. 607) from 1:4-diaminovaleric acid (ornithine). By combined methylation and oxidation this can yield succindialdehyde and methylamine, which can undergo condensation to $\begin{matrix} CH_2 \cdot CH(OH) \\ \vert \\ CH_2 \cdot CH(OH) \end{matrix}\!\!>\!NMe$. This product readily condenses with acetonedicarboxylic acid yielding:



which by loss of carbon dioxide gives:

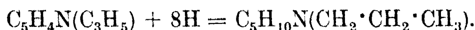


tropinone. By similar processes the formation of many alkaloids and derivatives of pyrrolidine, piperidine, quinoline, iso-quinoline, related to the alkaloids, can be explained.

A. Alkaloids derived from Pyridine

1. **Coniine,** dextro-rotatory *a-normal-propyl-piperidine,* $C_5H_{10}N(C_3H_7)$, is the poisonous principle of hemlock (*Conium maculatum*). It is a colourless dextro-rotatory liquid of stupefying odour, sparingly soluble in water, and boils at 167°. Hydriodic acid at a high temperature reduces it to normal octane, while nitric acid oxidizes it to butyric acid, and potassium permanganate to picolinic acid (hence the α-position).

Ladenburg has prepared it synthetically by reducing α-allyl-pyridine (p. 572) in alcoholic solution by means of sodium:



$$C_5H_4N(C_3H_5) + 8H = C_5H_{10}N(CH_2 \cdot CH_2 \cdot CH_3).$$

The pyridine ring is reduced to a piperidine ring, and at the same time the unsaturated allyl side-chain is reduced to a *n*-propyl group. The α-carbon atom is an asymmetric carbon atom, *i.e.* it is attached to four different monovalent radicals, and the whole molecule is asymmetric. The synthetical product is optically inactive, and thus differs from the natural product, but it has been resolved by fractional crystallization of the *d*-tartrate into *d*- and *l*-coniine. The relations of these two bases to one another and to the inactive modification are the same as those of *d*- to *l*-tartaric acid and to racemic acid.

2. The alkaloid, **pelletierine,** found in pomegranate bark, is an aldehyde, and has a CHO group in place of the terminal CH_3 group in coniine, and when reduced with sodium ethoxide at 160–170°, it yields *dl*-coniine (*Hess* and *Eichel,* B. 1917, **50,** 1192, 1386; 1918, **51,** 714).

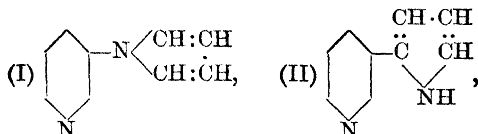
3. Alkaloids derived from pyridine are present in areca nut; these are **guvacine,** or 1:2:5:6-tetrahydropyridine-3-carboxylic acid, which has been synthesised by *Wohl* and *Losanitsch,* 1908; **guvacoline,** the corresponding methyl ester; **arecaine,** or arecaidine, the N-methyl derivative of guvacine; and **arecoline,** the methyl ester of arecaidine. (B. 1919, **52 B,** 206).

Ricinine, $C_8H_8O_2N_2$, an alkaloid from the castor-bean, is 1-methyl-2-keto-3-cyano-4-methoxy-Δ^1-dihydropyridine and has been synthesised by *Späth* and *Koller* (B. 1923, 2454).

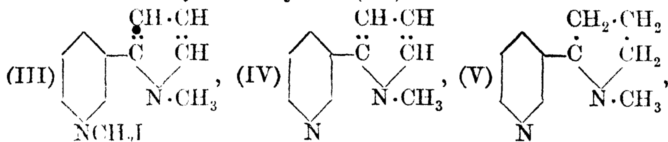
Nicotine, $C_{10}H_{14}N_2$, is the poisonous constituent of the tobacco plant, in which it exists in combination with malic and citric acids. It is a colourless, oily liquid soluble in water, and is lævo-rotatory. It rapidly oxidizes in contact

with the air, and boils at 247°. It is a di-tertiary base, as it combines with methyl iodide, yielding two isomeric quaternary salts. On oxidation with permanganate it yields nicotinic acid, and hence must be a β-pyridine derivative. These reactions, combined with its synthesis (*Pictet*, C. R. 1903, **137**, 860), prove it to be α-pyridyl-N-methyl-pyrrolidine (formula V).

Synthesis:—Nicotinic acid is transformed into its amide, and this with bromine and alkali (*Hofmann's* reaction, pp. 110, 191) gives β-amino-pyridine, the salt of which with mucic acid (p. 268) distilled yields N-pyridyl-pyrrole (I):

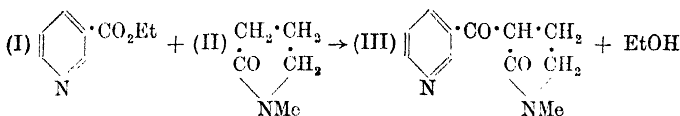


and the vapour of this passed through a heated tube gives the isomeric α-pyridyl-pyrrole (II), the potassium derivative of which with methyl iodide yields (III):



and when distilled with lime α-pyridyl-N-methyl-pyrrol (IV), which can be indirectly reduced to r-nicotine, and this may be resolved into its optically active components by the aid of d-tartaric acid when l-nicotine-d-tartrate crystallizes out first.

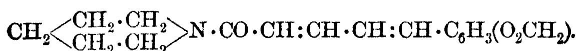
A simpler synthesis by *Späth* and *Bretschneider* (B. 1928, 327) is as follows: Ethyl pyridine-3-carboxylate (I):



condenses with 1-methyl-2-pyrrolidone (II) in the presence of sodium ethoxide yielding the bicyclic compound III, which with fuming hydrochloric acid yields the aminoketone $C_5H_5N \cdot CO \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot NHMe$ by hydrolysis and loss of

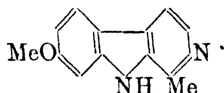
CO_2. The ketone reduced with zinc dust and alkali yields the corresponding secondary alcohol, and this reacts with fuming hydriodic acid yielding the iodide, $C_5H_5N\cdot CHI\cdot CH_2\cdot CH_2\cdot CH_2\cdot NHMe$, from which *dl*-nicotine is formed by the action of alkalis entailing the loss of hydrogen iodide and the closing of the pyrrolidine ring.

Piperine (p. 574), piperic acid piperidide, can be synthesised from piperoyl chloride and piperidine. It melts at 128°, is present in the fruits of different species of pepper, and on hydrolysis yields piperidine and piperic acid (p. 495).



For synthesis of piperic acid see *Ladenburg* and *Scholtz*, B. 1894, 1958.

The alkaloid **harmine** from the seeds of *Peganum harmala*, according to *Perkin* and *Robinson* (J. C. S. 1919, 933, 971; 1921, 1602; 1922, 1872), contains condensed benzene, pyrrole and pyridine nuclei and is represented by the formula:



B. Bases derived from Quinoline

Among these are the alkaloids present in **Cinchona** barks.

(*a*) **Quinine**, $C_{20}H_{24}O_2N_2 + 3H_2O$, a diacid base of intensely bitter taste and alkaline reaction, of which the sulphate and chloride are universally used as febrifuges. It crystallizes in prisms or silky glistening needles, melts at 177° when anhydrous, is sparingly soluble in water, and is lævo-rotatory. Dilute solutions of its salts show a brilliant blue fluorescence.

As a base quinine is a tertiary diamine, but it contains in addition—as its reactions show—one hydroxy-, one methoxy-group and an ethylene linking, and seems to be built up of two different ring systems:



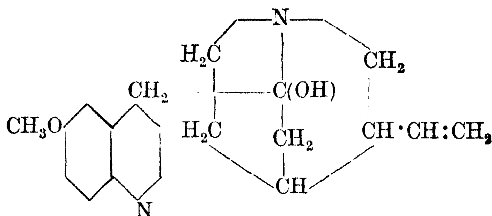
The first of these represents the radical of a 6-methoxy-

quinoline, and this compound is obtained when quinine is fused with potash. The second system probably possesses a ring similar to that of tropine, since it yields as decomposition products sometimes a pyridine derivative (*e.g.* β-ethyl-pyridine on fusion with alkali), and sometimes benzene derivatives containing no nitrogen (*e.g.* a phenolic compound, $C_{10}H_{12}OH$, together with ammonia, on successive treatment with phosphorus pentachloride, potash, and hydrobromic acid).

It yields quinic acid, 6-methoxy-quinoline-4-carboxylic acid, $C_9H_5N(OCH_3)CO_2H$ (p. 586), and meroquinene when oxidized with dichromate mixture.

Meroquinene appears to be 3-vinylpiperidyl-4-acetic acid (B. **30,** 1326), $CO_2H{\cdot}CH_2{\cdot}CH\left\langle\begin{matrix}CH(CH{:}CH_2){\cdot}CH_2\\ CH_2\text{———————}CH_2\end{matrix}\right\rangle NH$, as it yields first cincholoiponic acid, 3-carboxypiperidyl-4-acetic acid, and finally *loiponic acid*, piperidine-3:4-dicarboxylic acid, when oxidized with permanganate.

The formula suggested for quinine by *Koenigs* is:



and this has received support from *Rabe* and his co-workers, as both quinine and cinchonine when oxidized yield ketones containing the same number of C atoms. When heated with acetic acid the two alkaloids yield isomeric products known respectively as **quinotoxine** and **cinchotoxine** on account of their poisonous properties. These bases are ketones and secondary bases, and are formed by the conversion of the C(OH) group into CO and the rupture between the N atom and this C atom.

Quinine is a valuable drug in cases of malaria; numerous substitutes are now employed, especially quinine derivatives devoid of bitter taste. The esters derived from the alcoholic OH group—*aristoquinine*, diquinine carbonate; *euquinine*, ethyl quinine carbonate; and *saloquinine*, quinine salicylate—are used.

(*b*) **Cinchonine,** $C_{19}H_{22}ON_2$, is similar to quinine, but without the methoxy group in the quinoline nucleus. It crystallizes in colourless prisms, sublimes readily, and is not so active a febrifuge as quinine. When oxidized with dichromate and sulphuric acid it yields cinchoninic (quinoline-4-carboxylic) acid and meroquinene; with permanganate it yields cinchotenine and carbonic acid. Cinchotenine no longer combines with hydrogen chloride, and in the oxidation the double linking present in cinchonine has been removed and a carboxylic group introduced. When treated with PCl_5 and then with alcoholic potash, cinchonine loses a molecule of water, yielding *cinchene*, $C_{19}H_{20}N_2$, which can be hydrolysed by 25 per cent phosphoric acid to lepidine (4-methyl-quinoline) and meroquinene. It has very little therapeutic value.

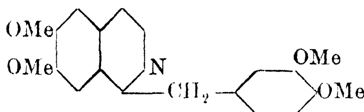
(*c*) *d*-**Quinidine,** $C_{20}H_{24}O_2N_2$, and **Cinchonidine,** $C_{19}H_{22}ON_2$, are probably stereoisomeric with quinine and cinchonine.

These are but a few of the numerous alkaloids present in these barks. In addition, organic acids (*e.g.* quinic and quinotannic) and neutral substances are also present.

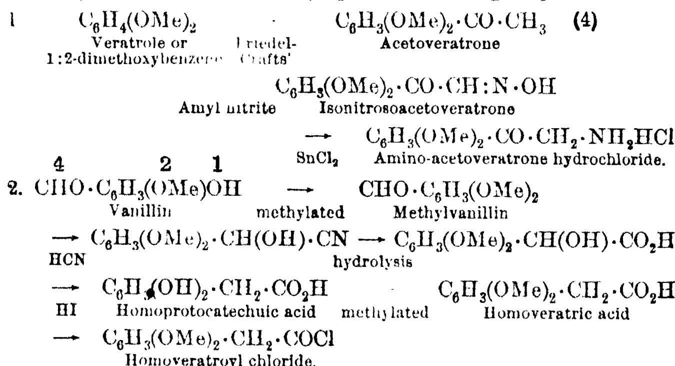
C. Bases derived from *Iso*-Quinoline

(*a*) **Papaverine,** $C_{20}H_{21}O_4N$, is found (1 per cent) together with narcotine, narceine, laudanosine, laudanine, and the morphine alkaloids in opium, the solid obtained by drying the juices extracted from the seed vessels of *Papaver somniferum*. In addition to some twenty alkaloids, many of which are present in only small quantities, opium also contains fats, resins, sugars, albumins, &c. The alkaloid crystallizes in prisms, m.-pt. 147°, and is optically inactive. It has hypnotic properties, but not to the same extent as morphine. It is a tertiary base, and all four oxygen atoms are present as methoxy groups, and when hydrolysed with hydriodic acid the corresponding tetrahydroxy-derivative, *papaveroline*, $C_{16}H_{13}O_4N$, is formed. When oxidized with permanganate it yields first *papaveraldine* $C_{20}H_{19}O_5N$, and finally dimethoxy-iso-quinoline-carboxylic acid and α-carbocinchomeronic acid (pyridine-1:2:3-carboxylic acid). When fused with potash it takes up two hydrogen atoms, and yields 4:5-dimethoxy-iso-quinoline and 3:4 dimethoxytoluene. When reduced, the N ring adds on 4 H atoms.

From these and other reactions *G. Goldschmudt* concluded that the base is 3:4-*dimethoxybenzyl*-4′:5′-*dimethoxy-iso-quinoline*:



and this formula has been confirmed by *Pictet* and *Gams*' synthesis (C. R. 1909, **149**, 210) by the following steps:—



3. Amino-acetoveratrone hydrochloride and homoveratroyl chloride condense in the presence of cold potassium hydroxide, yielding $(OMe)_2C_6H_3 \cdot CO \cdot CH_2 \cdot NH \cdot CO \cdot CH_2 \cdot C_6H_3(OMe)_2$; this can be reduced to the corresponding secondary alcohol which reacts with dehydrating agents, losing two molecules of water and forming 3′:4′-dimethoxybenzyl-4:5-dimethoxy-iso-quinoline, which is identical with papaverine.

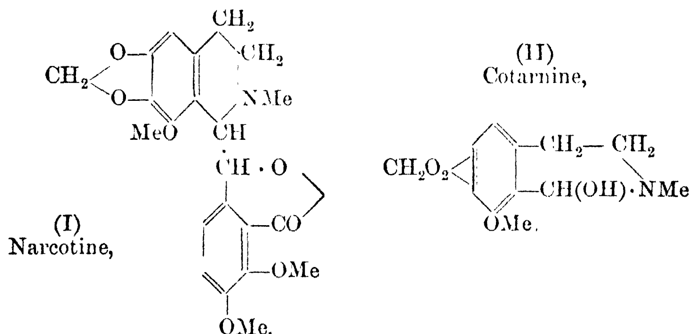
(*b*) **Laudanosine,** $C_{21}H_{27}O_4N$, crystallizes in needles, m.-pt. 89°, and is dextro-rotatory. It has been shown by *Pictet* and *Athanescu* (B. **33**, 2346) to be an N-methyl-tetra-hydropapaverine, and has been synthesised by *Pictet* and *Finkelstein* (C. R. 1909, **148**, 295).

Laudanine is the 3-hydroxy-4-methoxybenzyl compound corresponding with laudanosine (3:4-dimethoxybenzyl-) (M. 1921, 273).

(*c*) **Narcotine,** $C_{22}H_{23}O_7N$, occurs in opium (6 per cent), crystallizes in colourless needles, m.-pt. 176°, and is lævorotatory. It is a feeble tertiary base, and its salts are readily

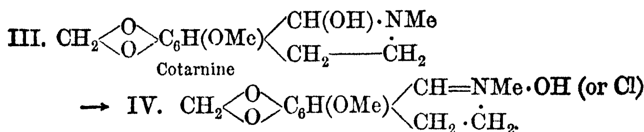
hydrolysed by water. It contains three methoxy groups, and when hydrolysed by dilute acids or alkalis, yields opianic acid and hydro-cotarnine. When reduced it yields meconine and hydro-cotarnine, and when oxidized yields opianic acid and cotarnine, and when heated with alkalis at 220° yields methylamines, thus indicating that the N-atom is methylated.

The *dl* compound (called **gnoscopine**) has been synthesised in small quantities (*Perkin* and *Robinson*, J. C. S. 1911, 776) by boiling an alcoholic solution of cotarnine and meconine, and has been resolved by means of *d*-bromo-camphor-sulphonic acid.

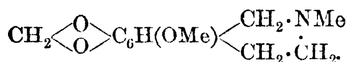


Both meconine (VII, p. 603), the lactone of 6-hydroxymethyl-2:3-dimethoxybenzoic acid, and cotarnine have been synthesised. The former by *Fritsch* (A. **301**, 352) and the latter by *Salway* (J. C. S. 1910, 1208), and also by *Decker* and *Becker* (A. 1913, **395**, 328).

The structural formula (II) was deduced by *Roser* for cotarnine by a study of its degradation products. When methylated and decomposed by alkalis it yields trimethylamine and an aldehyde, cotarnone, $C_9H_9O_3 \cdot CHO$, which on further oxidation gives a methoxy-dibasic acid, known as cotarnic acid, and this with hydriodic acid and phosphorus at 160° yields gallic acid (3:4:5-trihydroxybenzoic acid). Cotarnine itself, in ethereal or chloroform solution, has the carbonium structure III, whereas its salts and also the base in aqueous or alcoholic solution have the ammonium structure IV (cf. *Dobbie, Lauder,* and *Tinkler*, J. C. S. 1903, 598; 1904, 121):

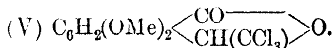


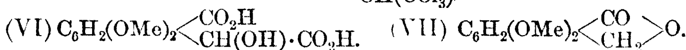
Cotarnic acid is 3-methoxy-4:5-methylenedioxyphthalic acid, and cotarnone 6-vinyl-3-methoxy-4:5-methylenedioxy-benzaldehyde. Hydro-cotarnine is also a reduced iso-quinoline derivative:



The steps in *Salway's* synthesis of cotarnine are: Myristic aldehyde (3-methoxy-4:5-methylenedioxy-benzaldehyde) $\xrightarrow{}$ 3-
Perkin's synthesis
methoxy-4:5-methylenedioxy-cinnamic acid → corresponding
red.
dihydro acid → acid amide → β-3-methoxy-4:5-methylene-
Hofmann reaction
dioxy-phenylethylamine → phenacetyl-derivative of amine → 8-methoxy-6 : 7-methylenedioxy-1-benzyl-3 : 4-dihydro-iso-quinoline → 1-benzylhydrocotarnine → cotarnine.
Methochloride with tin and HCl. $H_2SO_4 + MnO_2$.

Fritsch's synthesis of meconine consists in condensing chloral with the ester of 2:3-dimethoxybenzoic acid, hydrolysing the product (V) to the hydroxy dibasic acid (VI), and, finally, eliminating CO_2 and H_2O by heating the dibasic acid and obtaining the lactone, meconine (VII):

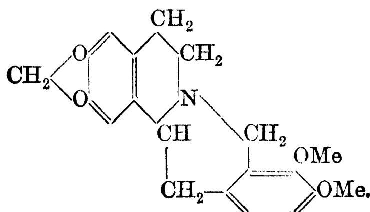




(*d*) **Hydrastine,** $C_{21}H_{21}O_6N$, occurs in the roots of *Hydrastis canadensis*, and differs from narcotine by having no methoxy group in the iso-quinoline ring. When oxidized it yields opianic acid and hydrastinine, which is the analogue of cotarnine. (Synthesis of hydrastinine, cf. *Fritsch*, A. 1895, **286,** 18).

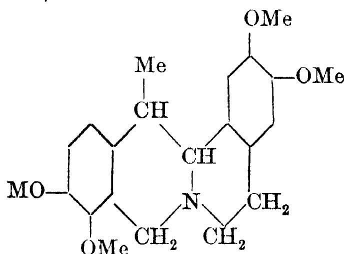
(*e*) **Berberine,** $C_{20}H_{17}O_4N, H_2O$, is the chief alkaloid present in *Hydrastis*, but has not marked physiological properties.

(*Perkin* and *Robinson*, J. C. S. 1910, 305; 1912, 1219; *Tinkler*, 1911, 1345; *Robinson*, 1917, 958.) Tetrahydroberberine is:



For its synthesis see *Pictet* and *Gams*, C. R. 1911, **153**, 386; also J. C. S. 1924, 1686. The positions of the double linkings in berberine are not known with certainty.

(*f*) **Corydaline,** $C_{22}H_{27}O_4N$, from *Corydalis cava*, crystallizes in prisms, m.-pt. 134·5°, and contains four methoxy groups. The formula below given by *Koepfli* and *Perkin* (J. C. S. 1928, 2989) differs slightly from that suggested by *Dobbie* and *Lauder* (1903, 605).



Emetine, cephaeline monomethyl ether, $C_{29}H_{40}O_4N_2$, and cephaeline are alkaloids present in ipecacuanha, and appear to be derived from iso-quinoline, as 6:7-dimethoxy-iso-quinoline-1-carboxylic acid is found among their oxidation products. The former is largely used for the cure of amœbic dysentery.

For absorption spectra of iso-quinoline alkaloids cf. *Dobbie* and *Fox*, J. C. S. 1914, **105**, 1639.

D. The Morphine Group of Bases

The three alkaloids morphine, codeine, and thebaine are characterized by containing a phenanthrene nucleus in addition to a nitrogen ring. They are all present in opium.

(*a*) **Morphine,** $C_{17}H_{19}O_3N$, constitutes on the average 10 per cent of opium. It crystallizes in small prisms ($+H_2O$), melting and decomposing at 230°, has a bitter taste, and is a valuable soporific. It is a mono-acid tertiary base, containing two hydroxyl groups, one of which is phenolic and the second alcoholic. When distilled with zinc dust it yields phenanthrene together with pyrrole, pyridine, and trimethylamine. Further proof of the presence of the phenanthrene nucleus has been afforded by the process of exhaustive methylation. With methyl iodide it yields codeine methiodide, formed by the methylation of the phenolic hydroxyl group and addition of methyl iodide to the tertiary N-atom. This product, with potassium hydroxide, loses hydrogen iodide and yields a tertiary base, *methylmorphimethine*, which with acetic anhydride gives 3-methoxy-4-hydroxy-phenanthrene (methylmorphol) and hydroxyethyldimethylamine, $OH \cdot CH_2 \cdot CH_2 \cdot NMe_2$. Different formulæ have been suggested by *Pschorr*, *Knorr*, *Braun*, and others. *Faltis* (Arch. Pharm. 1917, **255**, 85) gives a critical review of the different formulæ. Compare also *Gulland* and *Robinson*, J. C. S. 1923, 980; *Schöpf* and *Borkowsky*, A. 1927, **458**, 148.

(*b*) **Codeine,** $C_{18}H_{21}O_3N$, is a methyl derivative of morphine, and can be obtained from the latter by methylation of its phenolic group. When oxidized it yields the ketone *codeinone*, and this with acetic anhydride yields hydroxyethyl-methylamine and 3-methoxy-4:6-dihydroxy-phenanthrene.

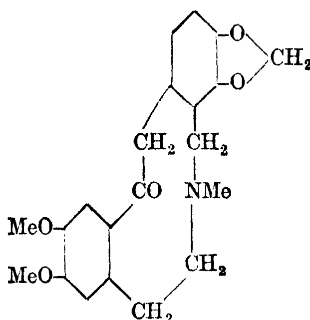
(*c*) **Thebaine** is morphine in which both hydroxyls are methylated. (Cf. *Freund* and *Speyer*, B. 1916, **49**, 1287.)

Numerous alkyl derivatives of morphine are manufactured and used as drugs in place of codeine. *Dionine* is ethylmorphine hydrochloride, *peronine* is benzylmorphine hydrochloride, *heroin* is diacetylmorphine.

For synthetical products allied to morphine see *Knorr*, A. **301**, 1; **307**, 171, 187; B. **32**, 732.

(*d*) **Cryptopine,** $C_{21}H_{23}O_5N$, and **protopine,** $C_{20}H_{19}O_5N$, present in small amounts in opium, have been investigated

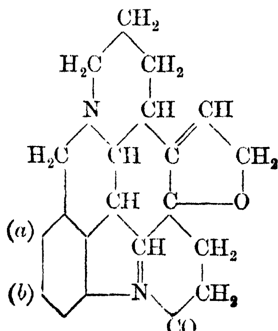
by *Perkin* (J. C. S. 1916, **109**, 815), who suggests the formula containing a 10-membered ring (1N + 9H) condensed with two benzene nuclei for cryptopine, which cannot be resolved into optically active modifications.



E. Strychnine Bases

Strychnos nux vomica and certain other beans contain:

(*a*) **Strychnine,** $C_{21}H_{22}O_2N_2$. This is excessively poisonous, produces tetanic spasms, crystallizes in four-sided prisms, and yields quinoline and indole when fused with potash, β-picoline when distilled with lime, and carbazole when heated with zinc dust. It is a mono-acid tertiary base, and melts at 284°. The formula suggested by *Fawcett, Perkin* and *Robinson*, J. C. S. 1928, 3082 is



(*b*) **Brucine,** $C_{23}H_{26}O_4N_2$, $4H_2O$, which crystallizes in prisms, and is converted into homologues of pyridine on fusion with potash. It is a dimethoxystrychnine with OMe in positions (*a*) and (*b*).

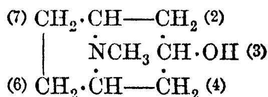
F. Solanine and Coca Bases

Atropine and hyoscyamine are isomeric bases of the formula $C_{17}H_{23}O_3N$, which can be respectively prepared from *Atropa Belladonna* (Deadly Nightshade) and *Datura Stramonium*, and which are remarkable for their mydriatic action (power of dilating the pupil of the eye).

Atropine crystallizes in colourless prisms or needles melting at 115°, possesses an extremely bitter taste, is optically inactive, and is hydrolysed by baryta water to *dl*-tropic acid (α-phenyl-β-hydroxy-propionic acid, $OH{\cdot}CH_2{\cdot}CHPh{\cdot}CO_2H$. p. 493) and tropine, $C_8H_{15}ON$, and is therefore the tropic ester of tropine. The alkaloid can be synthesised by evaporating a dilute hydrochloric acid solution of tropine and tropic acid. A complete synthesis of atropine has been accomplished, as both tropic acid and tropine have been synthesised.

When optically active (*d*- and *l*-) tropic acids are used, a dextro- and a lævo-rotatory atropine result) B. **22,** 2590). And if, instead of tropic acid itself, other organic acids are employed, homologous bases, the " **tropeïnes** ", are obtained; thus mandelic acid yields **homatropine,** $C_{16}H_{21}NO_3$, which exerts like atropine a mydriatic action, although a less lasting one, (*Ladenburg*, A. **217,** 82; *Jowett* and *Pyman*, J. C. S. 1909, 1090).

Tropine itself is a cycloheptanol with a nitrogen bridge:

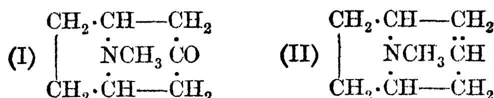


(*Willstätter*, B. 1898, **31,** 1538, 2498, 2655). For synthesis cf. *Willstätter*, A. 1901, **317,** 307; B. 1901, **34,** 129, 3163.

It is a tertiary base, crystallizes in plates, m.-pt. 62°, and b.-pt. 220°.

On oxidation it yields the ketone **tropinone** (I) and then **tropinic acid,** or 1-*methyl-pyrrolidine*-2-*carboxylic*-5-*acetic acid.*

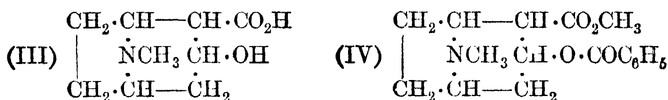
Concentrated hydrochloric acid converts it into **tropidine** (II),



an oily base distilling at 162°, and also obtainable by the elimination of carbon dioxide from anhydro-ecgonine.

Tropinone is readily synthesised from succindialdehyde, methylamine, and acetone, or calcium acetonedicarboxylate (*Robinson*, J. C. S. 1917, **111**, 762). For details see p. 595. Tropine is formed when tropinone is reduced with zinc dust and concentrated acid. It exists in two forms, tropine and the more stable ψ tropine, which are probably stereoisomeric. In the one case the Me and OH (of the ·CH·OH group) are on the same side of the plane of the ring and on the other the Me and H (of the CH·OH group on the same side.).

Ecgonine, or *tropine-carboxylic acid* (III),



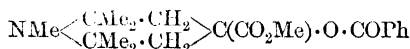
crystallizes with one molecule of water, and may be obtained by the hydrolysis of products contained in coca leaves. It melts at 198°, and is lævo-rotatory; and, on warming with alkalis, gives iso-ecgonine, which is dextro-rotatory. As an alcohol it forms a benzoyl derivative, and as an acid a methyl ester. (See Cocaine.) It is synthesised by the action of carbon dioxide on the metallic salts derived from tropinone (*Willstätter* and *Bode*, B. 1900, 411), and the reduction of the product with sodium amalgam in weakly alkaline solution.

Cocaine, or *benzoyl-l-ecgonine methyl ester* (IV) is the active constituent of the coca leaf (*Erythroxylon coca*); it melts at 98°, is lævo-rotatory, and is used in surgery as a local anæsthetic for deadening pain. It has been synthesised by benzoylating and esterifying ecgonine (B. 1885, **18**, 2953).

Hyoscyamine, which crystallizes in needles or plates, melting at 109°, resembles atropine closely, and is readily transformed into the latter under the influence of various alkalis (*Will*, B. **21**, 1725, 2777). In contact with water it is slowly

hydrolysed to *l*-tropic acid and inactive tropine. Atropine is racemic hyoscyamine.

Various substitutes for cocaine have been recommended, as its solutions do not keep well. *Willstätter* (B. **29**, 1575, 2216) obtained an isomeride of ecgonine by the addition of HCN to tropinone (I) and subsequent hydrolysis, and from this **α-cocaine** was obtained by benzoylation and esterification. α-Cocaine contains both CO_2Me and COPh groups attached to the same carbon atom and has no anæsthetic properties. **α-Eucaine** is a cheap substitute for cocaine prepared from triacetonamine, $NH<\begin{matrix}CMe_2\cdot CH_2\\CMe_2\cdot CH_2\end{matrix}>CO$ (p. 140, by addition of HCN, hydrolysis, benzoylation of the hydroxy-acid thus formed, and final methylation of the imino and carboxylic groups. Its structure is:



$$NMe<\begin{matrix}CMe_2\cdot CH_2\\CMe_2\cdot CH_2\end{matrix}>C(CO_2Me)\cdot O\cdot COPh$$

(*Merling*, 1897). Although more stable and less toxic than cocaine, it produces irritant effects when injected, and is now replaced by other synthetic products (cf. Chap. LIV, B.).

Scopolamine or **hyoscine,** present in *Datura meteloides*, is the tropyl ester of scopoline, and dihydroscopoline is related to tropine; it contains two hydroxyl groups in position 6 and 7 and none in position 3. When hydrolysed it yields oscine and tropic acid. Scopoline is the anhydride of 6:7-dihydroxy tropine, and oscine the isomeric 3:7 anhydride (J. C. S. 1919, 476, B. 1922, 1972.)

XLI. TERPENES AND CAMPHORS

For history of terpenes see *Tilden*, Science Progress, 1911, **6**, 46. Cf. *Wallach's* " Terpene and Camphor ", 1909.

Essential Oils.—Many plants, especially varieties of Coniferæ and of Citrus, contain, in their blossoms and fruits, oily substances to which they owe their peculiar fragrance or odour, and which can be obtained from them by distillation in steam or by pressure. These oils, " essential oils ", were formerly grouped together in a special class, but now they are recognized as being more or less heterogeneous; thus oil of bitter almonds is benzoic aldehyde, and Roman oil of cumin is a mixture of cymene and cumic aldehyde, &c. Many of these ethereal oils contain unsaturated hydrocarbons, which are usually termed **terpenes.** The common hydrocarbons met with have the general formula $C_{10}H_{16}$, and are spoken of as terpenes proper; but, in addition to these, hydrocarbons, represented by the formula C_5H_8 and known as **hemiterpenes,** exist. The commonest of these is **isoprene,** obtained by distilling caoutchouc. Hydrocarbons represented by the formula $C_{15}H_{24}$ are termed **sesquiterpenes,** and the more complex hydrocarbons, $(C_5H_8)_n$, **polyterpenes.** Certain ethereal oils consist chiefly of such hydrocarbons, *e.g.* turpentine, oil of citron, orange oil, and oil of thyme. Other oils contain appreciable amounts of oxygenated compounds, mainly of an alcoholic, ketonic or ester character, *e.g.* camphor and menthone, $C_{10}H_{16}O$, pulegone, &c. Many of these terpenes and ketones are reduced benzene derivatives, *e.g.* limonene, menthone; others again are more complex ring compounds, *e.g.* pinene and camphor. In addition to these two groups of compounds a third group has been discovered within recent years, namely, open-chain olefinic alcohols, aldehydes, or ketones, *e.g.* citronellal, geraniol, linalool.

The terpenes are widely distributed in the vegetable kingdom, especially in the Coniferæ (*Pinus, Picea, Abies,* &c.), in the varieties of Citrus, &c. The products which are isolated in the first instance from the individual plants, and which according to their source are designated terpene, citrene (from oil of citron), hesperidene (from oil of orange), thymene (from thyme, carvene (from oil of cumin), eucalyptene, olibene, &c., have for the most part the formula $C_{10}H_{16}$, and approximately

equal boiling-points (160°–190°); they are not, however, chemical individuals, but mixtures of isomeric compounds.

With the exception of camphene they are all liquid, but it is hardly possible to separate them completely by fractional distillation (see table, p. 623, for boiling-points). The terpenes can, however, be obtained chemically pure from crystalline derivatives. Quite recently, numerous compounds belonging to this class have been synthesised.

For simplicity the terpenes and allied oxygen compounds (camphors) may be divided into the following groups:—

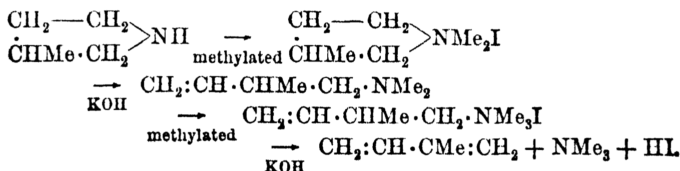
A. Open-chain olefinic compounds.
B. Monocyclic terpenes.
C. Complex cyclic terpenes.

Practically all the compounds dealt with in these three divisions could have been discussed under the aliphatic and cyclic compounds. A clearer view, however, of their relationships is obtained by bringing them together under the general heading of terpenes and camphors.

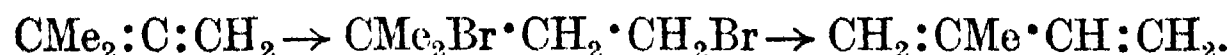
A. Open-chain Olefinic Terpenes and Camphors

Isoprene, the best-known hemiterpene, is a diolefine represented by the constitutional formula, $CH_2{:}CMe{\cdot}CH{:}CH_2$, 2-methyl-$\Delta^{1:3}$-butadiene. It is a colourless liquid, b.-pt. 37°, is formed by the dry distillation of rubber, or by decomposing turpentine at a dull red heat (cf. *Staudinger*, B. **44**, 2212). When boiled with an alcoholic solution of HCl it is converted into its isomeride dimethylallene $(CH_3)_2C{:}C{:}CH_2$. At 300° it undergoes polymerization to diisoprene (probably dipentene), and is transformed into products analogous to rubber when treated with concentrated hydrochloric acid or metallic sodium when kept for some time or when exposed to sunlight in the presence of traces of acid. Three syntheses of isoprene are of interest.

(*a*) From methyl-pyrrolidine by exhaustive methylation, p. 593 (*Euler*, J. pr. [2], **57**, 132):

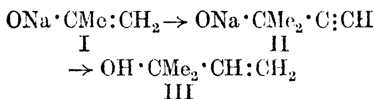


(*b*) From dimethyl-allene by the addition of two molecules of hydrogen bromide and subsequent elimination of the same (*Ipatieff*, *ibid.* **55**, 4):



$$CMe_2:C:CH_2 \rightarrow CMe_2Br \cdot CH_2 \cdot CH_2Br \rightarrow CH_2:CMe \cdot CH:CH_2.$$

(*c*) The sodium derivative of acetone I, obtained by the action of sodamide, reacts with acetylene yielding compound II, which on reduction gives III, from which isoprene is formed by the elimination of water (D. R. P.).

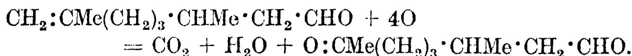


$$\underset{\text{I}}{ONa \cdot CMe:CH_2} \rightarrow \underset{\text{II}}{ONa \cdot CMe_2 \cdot C:CH}$$
$$\rightarrow \underset{\text{III}}{OH \cdot CMe_2 \cdot CH:CH_2}$$

Within recent years isoprene and butadiene derivatives generally have received marked attention on account of their relationships to synthetic rubber (Chap. LVI).

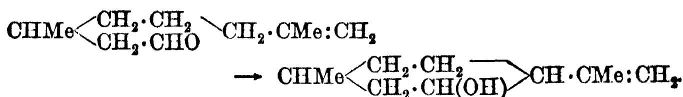
Practically all the natural products belonging to this group contain oxygen and are either aldehydes or alcohols.

Citronellal, $CH_2:CMe \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot CHMe \cdot CH_2 \cdot CHO$, is an example of an olefine aldehyde; it is present in citronella oil and also in lemongrass oil, together with citral and geraniol. It has b.-pt. 205°–208°. Its aldehydic nature is proved by the readiness with which it is reduced to a primary alcohol, citronellol, and oxidized to a monobasic acid, citronellic acid, containing the same number of carbon atoms. By oxidizing its dimethyl-acetal, *Harries* and *Schauwecker* (B. **34**, 1498, 2981) obtained a dihydroxy-derivative, thus proving the presence of an olefine linking; and on further oxidation with chromic anhydride they obtained the acetal of a keto-aldehyde containing nine carbon atoms, thus proving that the double bond is between the last and last but one carbon atoms with respect to the aldehyde group:

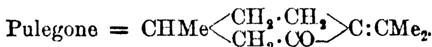


$$CH_2:CMe(CH_2)_3 \cdot CHMe \cdot CH_2 \cdot CHO + 4O$$
$$= CO_2 + H_2O + O:CMe(CH_2)_3 \cdot CHMe \cdot CH_2 \cdot CHO.$$

The positions of the methyl groups are proved by the relationship of the aldehyde to isopulegol, into which it is transformed when kept for some time, or more quickly when heated with acetic anhydride at 180°:

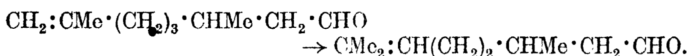


The constitution of pulegol follows from the fact that when oxidized it yields isopulegone, and this with baryta is transformed into pulegone by the wandering of an olefine linking.



An interesting reaction of citronellal is its oxidation in alkaline solution with permanganate, when it yields acetone and β-methyladipic acid, a result which would lead to the conclusion that the double bond is in position 5:6 with respect to the CHO group.

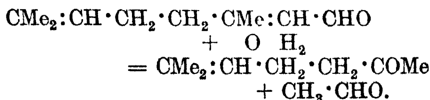
The only manner of reconciling this reaction with the reactions already given is the assumption that in the oxidation in alkaline solution a wandering of the double bond occurs:



Citral or **geranial**, $C_{10}H_{16}O$, occurs in both oil of lemons and of oranges, and may also be obtained by the oxidation of geraniol. Lemon-grass oil contains 70–80 per cent. It is a colourless oil, and distils at 110°–112° under 12 mm. pressure. Its constitution is represented as:

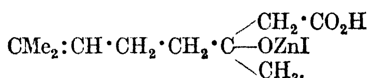


Its aldehydic nature follows from its reduction to **geraniol,** and its oxidation to an acid containing the same number of carbon atoms, namely, **geranic** acid. Its unsaturated character and the positions of the double bonds within the molecule follow from its general properties, but more especially (*a*) from its products of oxidation, viz. 2-methyl-Δ^2-heptenone, and carbon dioxide; (*b*) from its conversion into 2-methyl-Δ^2-heptenone and acetaldehyde by means of potassium carbonate or 1 per cent sodium hydroxide:



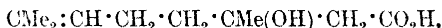
When heated with potassium hydrogen sulphate or glacial acetic acid, citral is converted into *p*-cymene by the elimination of $1H_2O$, addition of $2H_2O$ and final elimination of $3H_2O$, and with a primary amine yields cyclo α and β citrals.

Both citral and geranic acid have been synthesised by *Barbier* and *Bouveault* (C. R. 1896, **122**, 393). 2-Methyl-Δ^2-heptenone reacts with metallic zinc and iodo-acetic acid (*Reformatsky* reaction), yielding the compound:



$$CMe_2{:}CH\cdot CH_2\cdot CH_2\cdot C\begin{cases}CH_2\cdot CO_2H\\ OZnI\\ CH_3.\end{cases}$$

With dilute acid this yields the hydroxy-acid:



$$CMe_2{:}CH\cdot CH_2\cdot CH_2\cdot CMe(OH)\cdot CH_2\cdot CO_2H,$$

and when this is distilled with acetic anhydride, water is eliminated and geranic acid, $CMe{:}CH\cdot CH_2\cdot CH_2\cdot CMe{:}CH\cdot CO_2H$, formed.

Geranic acid with 70 per cent sulphuric acid yields α and β-cyclogeranic acids (2 : 6 : 6-trimethyl-Δ^2-cyclohexene-1-carboxylic acid and the isomeric Δ^1-acid).

Geranic acid, when reduced in the form of its ethyl ester with sodium and amyl alcohol, yields citronellic acid:



$$CH_2{:}CMe\cdot CH_2\cdot CH_2\cdot CH_2\cdot CHMe\cdot CH_2\cdot CO_2H,$$

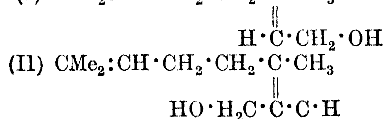
and when ethyl citronellate is reduced with sodium and alcohol, the corresponding primary alcohol, citronellol, is formed.

The citral obtained from lemon-grass oil contains 6–7 per cent of neral, β-citral, the aldehyde corresponding with nerol. The odour of this resembles that of citral, but is not quite so pleasant.

Geraniol, $C_{10}H_{18}O$, is the alcohol corresponding with α-citral, and is the chief constituent (90 per cent) of Indian geranium oil and of palma-rosa oil, which are largely used for adulterating rose oil. Its constitution follows from its relationship to citral and geranic acid, into which it is readily oxidized.

By reducing ordinary citral with alcohol and sodium amalgam, two stereoisomeric alcohols, geraniol and neral, are obtained, and these yield mixtures of citral and neral when reoxidized. Both alcohols yield terpineol by the action of acetic acid containing 1 to 2 per cent of sulphuric acid, but

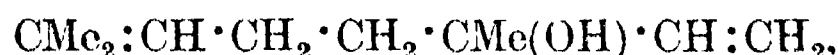
nerol reacts about nine times as readily as geraniol. The formation of terpineol can be accounted for by the addition and withdrawal of water. The two alcohols, geraniol and nerol, are represented respectively by the two formulæ I and II.

Both are optically inactive, and formula II is given to nerol on account of the readiness with which it yields terpineol. Geraniol reacts with HI yielding a moniodo derivative, $CMe_2I\cdot[CH_2]_3\cdot CMe:CH\cdot CH_2\cdot OH$, which loses HI in contact with alcoholic sodium hydroxide, giving a theoretical yield of **nerol,** whose tetrabromide melts at 118°, whereas geraniol tetrabromide melts at 70°.

Nerol has a distinct rose-like odour, different from that of geraniol. Its structural formula follows from its formation from the additive compound of geraniol and hydrogen iodide, and also from the fact that the corresponding aldehyde, neral, yields the same products as citral when heated with dilute alkalis (cf. p. 613).

Linalool or **coriandrol** is isomeric with geraniol, into which it is readily transformed by the action of dilute organic acids. It occurs as linalyl acetate in lavender, sage, and coriander oils, and is an important odoriferous principle in many essential oils. It is optically active, reacts as a tertiary alcohol, and hence is structurally- and not stereo-isomeric with geraniol. Its reactions agree best with the formula:



$$CMe_2:CH\cdot CH_2\cdot CH_2\cdot CMe(OH)\cdot CH:CH_2,$$

and its conversion into geraniol probably depends upon the addition and subsequent removal of water, the glycol,

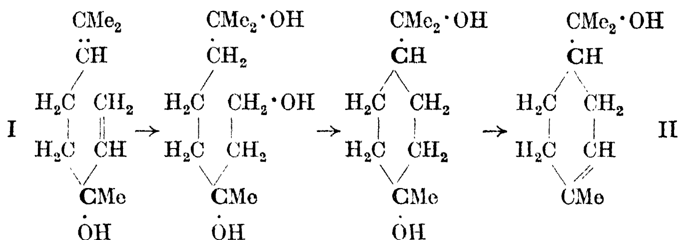


$$CMe_2:CH\cdot CH_2\cdot CH_2\cdot CMe(OH)\cdot CH_2\cdot CH_2\cdot OH,$$

being formed as the intermediate product. *l*-Linalool reacts with acetic anhydride, yielding nerol, geraniol, and *d*-terpineol.

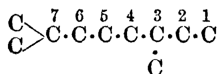
The formation of the last in an optically active form is of interest as the asymmetry of the *l*-linalool I and *d*-terpineol II

molecules is due to the presence of different asymmetric carbon atoms in the two molecules, as shown by the scheme in which asymmetric carbon atoms are given in heavy type.

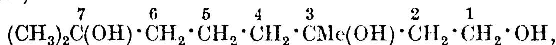


Isolinalool, $CMe_2 : CH \cdot CH_2 \cdot CH_2 \cdot CMe(OH) \cdot CH : CH_2$, is formed by the action of alkalis on geraniol trihydrobromide, $CH_3 \cdot CMeBr \cdot [CH_2]_3 \cdot CMeBr \cdot CH_2 \cdot CH_2Br$.

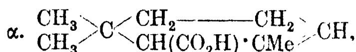
Compounds of this type with the carbon system:

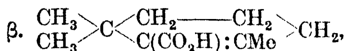


are readily transformed into derivatives of *p*-cymene by union between carbon atoms numbers 1 and 6, or into tetrahydrobenzene derivatives by union of numbers 2 and 7. Examples of the first type are (*a*) conversion of citral into *p*-cymene (p. 614); (*b*) conversion of geraniol into terpin or terpineol by heating with 10 per cent sulphuric acid. The trihydroxy alcohol,



is first formed, and ring closure takes place by the elimination of H attached to C No. 6 with OH attached to C No. 1. Examples of the second type are (*a*) formation of ionone (p. 638); (*b*) the conversion of geranic acid into *α* and *β* cyclo geranic acids (p. 614).





and similarly the conversion of citral into *α* and *β* cyclocitrals.

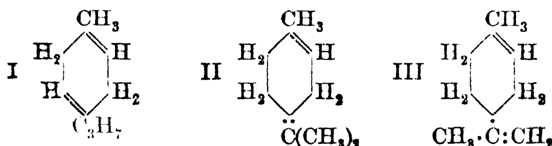
B. Monocyclic Terpenes and Camphors

I. **Terpenes.**—Many of the compounds are to be regarded as hydro-derivatives of cymene (p. 380). Their close relationship to cymene can be shown in very different ways: *e.g.* (*a*) the hydrocarbon **terpinene** when heated with iodine is transformed into *p*-cymene, *i.e.* *p*-methyl-isopropyl-benzene; (*b*) the ketone **carvone** when heated with mineral acids yields carvacrol, *i.e.* 1-methyl-2-hydroxy-4-isopropyl-benzene (p. 446); (*c*) on oxidation many terpenes yield terephthalic acid; (*d*) when brominated and then reduced many monocyclic terpenes yield benzene hydrocarbons (B. 1898, **31,** 2068). (*e*) Heating with sulphur usually removes the excess hydrogen as hydrogen sulphide and a substituted benzene hydrocarbon, usually cymene, is formed (*Vesterberg*, B. 1903, 4200).

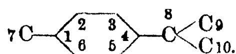
The unsaturated nature of these compounds follows from the readiness with which they form additive compounds; they yield **dihydrochlorides,** $C_{10}H_{18}Cl_2$, **tetrabromides,** $C_{10}H_{16}Br_4$, **nitroso-chlorides,** $C_{10}H_{16}(NOCl)_2$, **nitrosites,** $C_{10}H_{16}(NO)(NO_2)$, and **nitrosates,** $C_{10}H_{16}N_2O_4$. These compounds are of considerable importance, as most of them are well-defined crystalline compounds with definite melting-points, and can therefore be made use of in separating and identifying the various liquid terpenes. The nitroso-chlorides were first prepared by *Tilden* (J. C. S. 1877, 554), by the direct action of nitrosyl chloride, but are now usually obtained by *Wallach's* method, viz. by the action of a mixture of ethyl nitrite, acetic and hydrochloric acids on the hydrocarbon. The nitrosites are usually obtained by the action of sodium nitrite and acetic acid on the hydrocarbon, and the nitrosates by the direct addition of nitric peroxide or by the action of amyl nitrite and concentrated nitric acid. An interesting group of compounds are the **nitrolamines,** obtained by the action of amines (piperidine or benzylamine) on the nitroso-chlorides. They contain the NHR-group in place of the chlorine of the nitroso-chlorides. Such compounds crystallize well, and can be used for identifying the various terpenes.

All these reactions point to the presence (*a*) of a six-membered carbon ring in the monocyclic terpenes; (*b*) to the presence of two side chains, usually in *p*-positions, one consisting of the CH_3-group, and the second containing the grouping

$—C<^{C}_{C}$; (*c*) to the presence of two double bonds in the molecule. These may be both in the carbon ring, or one in the ring and one in a side chain, *e.g.*:



Fourteen such isomerides are theoretically possible. The carbon atoms are usually numbered as follows:



The saturated compound $C_{10}H_{20}$, viz. *p*-methyl-isopropyl-hexamethylene, is called **terpane***, and the compounds $C_{10}H_{16}$ are **terpadienes.** I is Δ-1:4-terpadiene, II is Δ-1:4 (8)-terpadiene, and III Δ-1:8 (9)-terpadiene.

The double linking in No. II between a carbon atom in the ring and a carbon of a side chain is termed a *semicyclic* linking. Such an unsaturated linking is quite stable under the influence of heat, but in the presence of acids it wanders into the nucleus, *e.g.* $\Delta^{4(8)}$ *p*-menthene is readily transformed into Δ^3 *p*-menthene.

A few of the terpenes contain the methyl- and isopropyl-groups in the meta positions, *e.g.* sylvestrene; such compounds are termed *m*-terpadienes.

The nitroso-chlorides are frequently colourless, and then appear to be bimolecular; some give blue solutions containing the monomolecular form. Compounds with a semicyclic linking $>C:CR_2$ yield unimolecular blue nitroso-chlorides volatile with steam. The blue compounds are true nitroso-compounds. When the NO-group becomes attached to $>CH$ it usually passes over into the isonitro-group $>C:N\cdot OH$, and the compound becomes colourless.

* The name **menthane** is sometimes used for this hydrocarbon and **menthadienes** for the terpadienes.

The following hydrocarbons belong to this group:

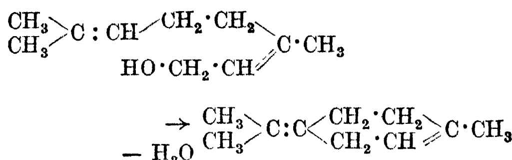
Dipentene, Δ-1:8(9)-terpadiene or **inactive limonene** (see formula III; for constitution cf. B. 1895, **28,** 2145; 1898, **31,** 1402; 1900, **33,** 1457). It occurs together with cineol in *Oleum cinæ*, and is prepared by heating pinene, camphene, sylvestrene, or limonene to 250°–270° for several hours, and also by the abstraction of hydrogen chloride from its dihydrochloride. It is further produced from pinene under the influence of dilute alcoholic sulphuric acid, from terpin hydrate and terpineol by the elimination of water, by the polymerization of isoprene, and, together with the latter substance, on distilling caoutchouc. Its formation from isoprene, $CH_2:C(CH_3)\cdot CH:CH_2$, by heating at 300° is a synthesis, since isoprene has been synthesised (p. 611). It is a liquid of pleasant odour like that of oil of citron, boils at 175°–176°, and is more stable than pinene, although it can still be transformed into terpinene by acids. It readily forms dipentene dihydrochloride with hydrochloric acid, and with bromine a crystalline tetrabromide melting at 125°. Its (inactive) nitroso-chloride yields, by the elimination of hydrogen chloride, the so-called **nitroso-dipentene** (inactive carvoxime), melting at 93°.

d-**Limonene,** *hesperidene, citrene,* or *carvene.* The oil of the orange rind consists almost entirely of dextro-limonene, which is also the chief constituent of carvene, oil of dill, oil of erigeron, &c.; oil of citron consists mainly of *d*-limonene and pinene. It boils at 175°, and forms a dextro-rotatory tetrabromide, $C_{10}H_{16}Br_4$, which melts at 104°. The dextro- and lævo-tetrabromides are identical, except that their crystals are the mirror images of one another. Dextro-limonene is very readily racemized to dipentene.

l-**Limonene** is present together with lævo-pinene in the oil of fir cones.

l- and *d*-limonenes yield nitroso-chlorides, $C_{10}H_{16}NOCl$, of corresponding rotatory powers; and, on the elimination of hydrogen chloride from these, *l*- and *d*-**nitroso-limonenes,** $C_{10}H_{15}NO$, which are identical with the carvoximes.

The conversion of geraniol into dipentene by means of formic acid, is a simple case of dehydration and ring closure, and the subsequent conversion of the $\Delta^{4(8)}$ linkage into a $\Delta^{8(9)}$ linkage, cf. p. 613,



It is interesting to note that the terpene present in essential oils rich in geraniol or citrol is limonene or dipentene.

Dipentene readily combines with hydrogen chloride, yielding a **dihydrochloride,** $C_{10}H_{18}Cl_2$, which melts at 50°. The same compound is also formed by the action of hydrogen chloride on limonene or on pinene, and when left in contact with aqueous alcohol yields terpin hydrate, $C_{10}H_{18}(OH)_3$ (cf. p. 625), in the form of large rhombic crystals melting at 117°.

Terpinene, probably Δ-1:3-*terpadiene*, is one of the most stable of the terpenes. It may be obtained by the action of alcoholic sulphuric acid on dipentene, or on other compounds which yield dipentene as an intermediate product, *e.g.* by shaking pinene with concentrated sulphuric acid, or by boiling terpin hydrate with dilute sulphuric acid. It boils at 179°–181°, is optically inactive, and most of its derivatives are oils, with the exception of the nitrosite, which melts at 155°.

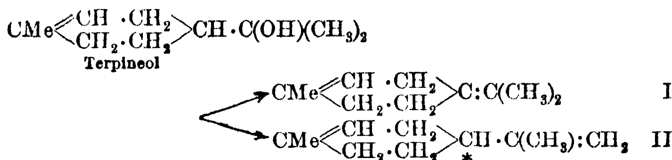
Terpinolene, Δ-1:4 (8)-*terpadiene*, is formed when terpineol is boiled for a short time with oxalic acid solution. It boils at 183°–185°, and is readily transformed by acids into terpinene. It forms a blue nitroso-chloride.

Sylvestrene, *Carvestrene*, Δ-1:8 (9)-*m-terpadiene*, b.-pt. 175°, is the chief dextro-rotatory constituent of Swedish and Russian oil of turpentine. It is one of the most stable of the terpenes, and gives a magnificent blue coloration with acetic anhydride and concentrated sulphuric acid. The CH_3 and C_3H_5 substituents are in the *m*-positions, as treatment with bromine converts it into *m*-cymene.

It has been synthesised from *m*-hydroxybenzoic acid by *Perkin* and *Tattersall* (J. C. S. 1907, 480) by reducing to its hexahydro derivative, oxidizing to γ-ketohexahydrobenzoic acid, and proceeding as in the synthesis of terpineol.

The constitution of dipentene is derived from its relationship to terpineol (p. 624) from which it is obtained by the elimination of water. If molecular rearrangement does not

occur during this reaction, it is clear that dipentene must have a constitutional formula corresponding with I or II.



Formula I is not dissymmetric, and therefore cannot represent the molecules of *d*- and *l*-limonenes and of dipentene; formula II, on the other hand, contains an asymmetric carbon atom, the one indicated by an asterisk, the molecule is dissymmetric, and can form *d*-, *l*-, and *r*-modifications.

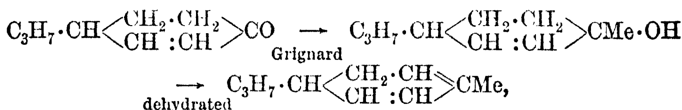
The correctness of formula II is confirmed by a study of some of the reactions of dipentene.

Dipentene forms a nitroso-chloride (colourless), and this with alkalis gives the oxime of carvone. The oxime when hydrolysed yields carvone, and this on reduction yields dihydrocarveol, a secondary alcohol formed by the addition of two atoms of hydrogen to one of the ethylene linkings and two atoms of hydrogen to the carbonyl group. Dihydrocarveol when oxidized yields a ketonic alcohol, $CH_3 \cdot C_6H_9(OH) \cdot CO \cdot CH_3$, proving the presence of the $\cdot C(CH_3):CH_2$ group in dihydrocarveol, carvone, and dipentene.

Terpinolene is also formed from terpineol by the elimination of water, and should therefore be represented by formula No. 1, a formula which is in harmony with the inactivity of the hydrocarbon. The stable terpinene most probably contains conjugate double bonds, and, as it is formed from terpinoline by the action of acids, it is Δ-1:3-terpadiene.

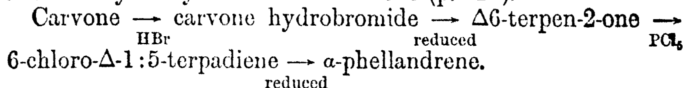
Phellandrene.—Three isomeric phellandrenes exist in nature: *d*-*α*-phellandrene in oil of bitter fennel and in elemi oil, *l*-*α*-phellandrene in Australian eucalyptus oil (*Eucalyptus amygdalina*), and *d*-*β*-phellandrene in water dropwort (*Phellandrium aquaticum*). The *d*- and *l*-*α*-phellandrenes are optical antipodes, and are both Δ-1:5-*terpadienes*. The b.-pt. is 62°/12 mm. It is transformed into terpinene by the action of acids, and its dibromide with alkalis yields cymene. This constitution follows from the fact that nitro-*α*-phellandrene, when carefully reduced, yields active carvotanacetone, Δ-5-terpene-2-one, and

has been confirmed by the synthesis of α-phellandrene from 4-isopropyl-Δ2-hexene-1-one (A. 359, 285):



$$C_3H_7\cdot CH<\begin{smallmatrix}CH_2\cdot CH_2\\ CH:CH\end{smallmatrix}>CO \xrightarrow[\text{Grignard}]{} C_3H_7\cdot CH<\begin{smallmatrix}CH_2\cdot CH_2\\ CH:CH\end{smallmatrix}>CMe\cdot OH$$
$$\xrightarrow[\text{dehydrated}]{} C_3H_7\cdot CH<\begin{smallmatrix}CH_2\cdot CH\\ CH:CH\end{smallmatrix}>CMe,$$

and also by its synthesis from carvone (p. 624).



Carvone $\xrightarrow[\text{HBr}]{}$ carvone hydrobromide $\xrightarrow[\text{reduced}]{}$ Δ6-terpen-2-one $\xrightarrow[PCl_5]{}$ 6-chloro-Δ-1:5-terpadiene $\xrightarrow[\text{reduced}]{}$ α-phellandrene.

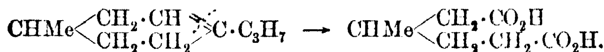
β-Phellandrene is Δ-2:1(7)-*terpadiene.* It has boiling-point 57°/11 mm., yields two nitrosites, melting-points 97° and 102°. Its constitution is based on the fact that it is oxidized by atmospheric oxygen to 4-isopropyl-Δ-2-hexene-1-one (A. **343,** 29), and on its synthesis from carvone (J. pr. **72,** 193; **75,** 141).

Carvone $\xrightarrow[\text{reduced}]{}$ carvomenthol (terpane-2-ol) $\xrightarrow[\text{dehydrated}]{}$ Δ-1-terpene $\xrightarrow[\text{bromine}]{}$ terpenedibromide $\xrightarrow[\text{alc. potash}]{}$ β-phellandrene, or from 4-isopropyl-Δ2-cyclohexene-1-one by condensing with ethyl bromoacetate and zinc, and finally eliminating CO_2 and H_2O.



$$>C:O \rightarrow >C(OH)\cdot CH_2\cdot CO_2H \rightarrow >C:CH_2.$$

Menthene, obtained from menthol by the elimination of water, is Δ-3-terpene; when oxidized it yields a glycol, which on further oxidation gives β-methyladipic acid:



$$CHMe<\begin{smallmatrix}CH_2\cdot CH\\ CH_2\cdot CH_2\end{smallmatrix}>C\cdot C_3H_7 \rightarrow CHMe<\begin{smallmatrix}CH_2\cdot CO_2H\\ CH_2\cdot CH_2\cdot CO_2H.\end{smallmatrix}$$

It has been synthesised by *Wallach* (B. **39,** 2504) by condensing 1-methylcyclohexan-4-one with ethyl α-bromoisobutyrate and zinc, hydrolysing and eliminating CO_2 and water.

A synthetical terpene or **dihydro-cymene** boiling at 174° has been prepared from succinylo-succinic ester (pp. 371, 501) (B. **26,** 233). It shows the complete terpene character.

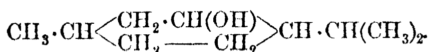
Most of these terpenes undergo oxidation on exposure to moist air, *i.e.* they undergo autoxidation. Thus limonene yields carvone, carveol, and other products (B. 1914, **47,** 2623)

SUMMARY OF DERIVATIVES

	Boiling-point.	Tetra-bromide. M.-p.	Dihydro-chloride. M.-p.	Nitrosite. M.-p.
Limonene......	175°	104°	50°	...
Dipentene......	175°	125°	50°	...
Terpinolene...	183°–185°	116°	...	...
Terpinene......	179°–181°	oil	oil	153°
Phellandrene..	171°–172°	oil	oil	105°
Sylvestrene....	175°	135°	72°	...

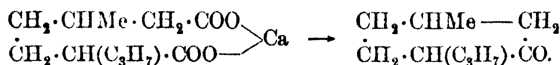
II. Camphor Compounds.—Alcohols and Ketones

Menthol, *3-terpanol,* mint camphor, $C_{10}H_{20}O$:



The *l*-modification is the chief constituent of oil of peppermint. It melts at 43°, has a strong odour of peppermint, and is used as an antiseptic and anæsthetic. When heated with copper sulphate it yields cymene, when reduced with hydriodic acid, hexahydrocymene, and on oxidation with permanganate it yields β-methyladipic acid, and several fatty acids. As the formula contains three asymmetric carbon atoms, several stereo-isomerides are possible.

The corresponding ketone **menthone,** *3-terpanone,* $C_{10}H_{18}O$, is obtained when the alcohol is oxidized with dichromate (*Beckmann,* A. 1891, **262,** 31), and also occurs in oil of peppermint. It boils at 207°, and has the characteristic properties of a ketone; its **semicarbazone** melts at 184°. It is readily converted into thymol (1-methyl-3-hydroxy-4-isopropyl-benzene) by bromination and elimination of hydrogen bromide, and when oxidized yields β-methyladipic acid. Hence follows the constitution, which is supported by its synthesis by the distillation of calcium β-methyl-α′-isopropylpimelate (*Kötz* and *Schwarz,* A. **357,** 206):



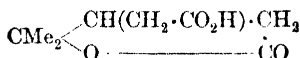
An unsaturated ketone, **pulegone,** *Δ-4(8)-terpene-3-one,* obtained from oil of pennyroyal, is isomeric with camphor, and on reduction yields menthone. Its constitution follows from the fact that when heated with water it yields acetone and 1-methylcyclohexan-3-one.

d-**Piperitone,** Δ^1-terpene-3-one, occurs (80 per cent) in the oil of the grass *Andropogon Jwarancusa* and the corresponding *dl*-compound in oils from certain species of eucalyptus (J. C. S. 1921, 779, 1644).

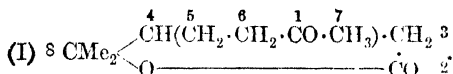
Carvone, Δ-6:8 (9)-*terpadiene-2-one*, is the chief constituent of oil of carraway seeds, and is widely distributed in the vegetable kingdom. It is a liquid, distils at 228°, exists in *d*-and-*l*-modifications, and has the properties of an unsaturated ketone (cf. A. 1897, **297**, 122). With hydroxylamine it yields carvoxime, which is identical with nitroso-limonene. When heated with phosphoric acid carvone yields carvacrol.

Terpineol, Δ-1-*terpene*-8-*ol*, does not occur in large quantities naturally, but is obtained readily from natural products, *e.g.* by the action of dilute potash on limonene hydrochloride, or by the hydration of pinene hydrate. It has m.-pt. 37°, b.-pt. 218°, and $[\alpha]_D - 106°$. When treated with dilute acids it can give dipentine, terpinolene, terpinene, terpin hydrate, cineol or cymene, according to the conditions. Its constitution is of importance, as those of several terpenes are deduced from that of terpineol. The constitution is based on (1) examination of its decomposition products, (2) its synthesis.

By means of dilute permanganate two hydroxyls are added to the double bond, and 1:2:8-trihydroxyterpane (trihydroxy-hexahydro-*p*-cymene) is formed, and this on further oxidation yields a ketolactone, homoterpenylic methyl ketone (by the fission at C atoms 1 and 2), which can be oxidized to acetic and terpenylic acids. The constitution of the latter has been proved to be:

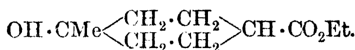


from its method of synthesis (*Simonsen*, J. C. S. 1907, 184).

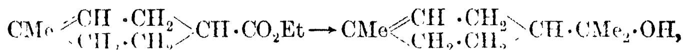


Homoterpenylic methyl ketone must have the formula I, and hence the 1:2:8-positions of the three hydroxyl groups in the first oxidation product, and the Δ-1-position of the ethylene linking and position 8 of the hydroxyl group in terpineol.

Its synthesis (*Perkin*, J. C. S. 1904, 654, is from δ-keto-hexahydrobenzoic acid (δ-keto-cyclohexane-carboxylic acid). The ester of this acid reacts with magnesium methyl iodide, and then with water, yielding:



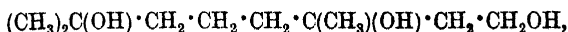
By the action of fuming hydrobromic acid the hydroxyl is replaced by bromine, and then by the action of pyridine hydrogen bromide is eliminated and Δ-3-tetrahydro-*p*-toluic acid is formed. The ethyl ester of this acid reacts with magnesium methyl iodide, and then with water, in the normal manner, yielding the tertiary alcohol, inactive terpineol:



and by the elimination of water dipentene is obtained.

This method of synthesis has been extended by *Perkin* and his students to a large number of cases, and they have obtained alcohols and unsaturated hydrocarbons analogous to the natural products, but which, so far, have not been obtained naturally. From Δ-1-tetrahydro-*p*-toluic acid, Δ-3-*p*-terpen-8-ol, and Δ-1:8 (9) terpadiene. From hexahydro-*o*-toluic acid, compounds similar to terpineol and dipentene were obtained, but with the substituents in *o*-positions. From hexahydrobenzoic acid a compound was obtained analogous to dipentene, but without the methyl substituent in position 1. By using optically active Δ-1-tetrahydro-*p*-toluic acid, an active alcohol and terpene were synthesised. (J. C. S. 1905, 639, 655, 661, 1067, 1083; 1906, 832, 839; 1908, 573, 1871, 1876; 1910, 2129, 2147; 1911, 118, 518, 526, 727, 741. For another method of synthesis of hydrocarbons allied to terpenes cf. *Haworth* and *Fyfe*, J. C. S. 1914, 1659).

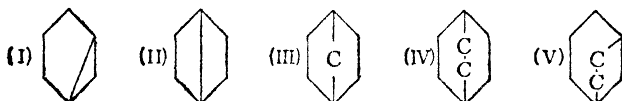
Terpin, *p-terpa*-1:8-*diol*, has been synthesised by the action of magnesium methyl iodide on both carbonyl groups of ethyl cyclohexanone-4-carboxylate (*Kay* and *Perkin*, J. C. S. 1907, 372), and is also formed by boiling terpineol with dilute sulphuric acid. It exists in two stereoisomeric modifications, *cis* and *trans*. The *cis* is the common form, and combines with water to give **terpin hydrate,** $C_{10}H_{22}O_3$,



which forms well-developed crystals, m.-pt. 116°. When dehydrated the terpins yield terpinene, terpinolene, terpineol, and **cineol** (p. 637).

C. Complex Cyclic Terpenes and Camphors

The compounds belonging to this group are bicyclic, *i.e.* the molecule is built up of two rings. Benzene or reduced benzene derivatives containing a diagonal linking in the *m*- or *p*-position (examples I and II) are bicyclic, also the compounds which can be regarded as derived from a single ring by the introduction of a *bridge* consisting of one or more carbon atoms (examples III, IV, and V). For systematic nomenclature cf. *Baeyer*, B. **33,** 3771; *Grignard,* Bull. Soc., 1912, **11,** 124; *Behal,* ibid. 264; *Büchner* and *Weigand,* B. 1913, **46,** 2108.



I. **Terpenes.**—*a*-**Pinene,** $C_{10}H_{16}$, is the chief constituent of German and American oil of turpentine, oil of juniper, eucalyptus, oil of sage, &c. It forms, together with *β*-pinene, sylvestrene, and dipentene, Russian and Swedish turpentine oil.

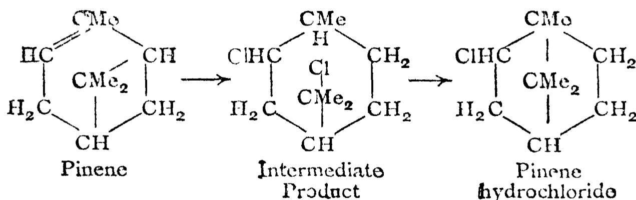
Oil of turpentine is obtained by distilling turpentine, the resin of pines, with steam, colophonium (fiddle resin) remaining behind. It is a colourless, strongly refracting liquid of characteristic odour, almost insoluble in water, but readily soluble in alcohol and ether. It dissolves resins and caoutchouc (being therefore used for the preparation of oil paints, lakes), also sulphur, phosphorus, &c. Pinene absorbs oxygen from the air with the formation of H_2O_2 and production of resin, minute quantities of formic acid, cymene, &c., being formed at the same time. Dilute nitric acid gives rise either to terephthalic acid in addition to fatty acids, or—under other conditions—to terpenylic acid (p. 624), $C_8H_{12}O_4$ (which belongs to the fatty series). Heating with iodine transforms it into cymene, the action being violent. It acts as an antiseptic, and arrests the secretions (*e.g.* that of the kidneys).

It exists in three stereoisomeric modifications: *d*-pinene or australene occurs in large quantities in German, Russian, and

Swedish oils; *l*-pinene or terebenthene in French turpentine oil; *d*-*l*-pinene is obtained by heating pinene nitroso-chloride with aniline:

	$[\alpha]_D^{20°}$		B.-pt.		$d_4^{20°}$
d........	+45°	....	156°	....	0·858
l........	−43·4°	....	156°	....	0·858
d-*l*......	0°	....	156°	....	0·858

Pinene has all the characteristic properties of an unsaturated compound. It forms a **nitroso-chloride** $(C_{10}H_{16}, NOCl)_2$, colourless crystals melting at 103°, which is used for isolating pinene from mixtures; also a **hydrochloride,** $C_{10}H_{17}Cl$, a white crystalline solid melting at 131°, with a camphor-like odour, hence the name "artificial camphor". This is insoluble in water, but readily soluble in alcohol, and if hydrogen chloride is eliminated by weak alkali, *e.g.* by heating it with soap or with silver acetate, camphene is obtained. It is identical with bornyl chloride, and on oxidation yields camphoric and apocamphoric acid. It is probable that by conversion into the hydrochloride an intramolecular rearrangement has taken place, as indicated by the following formulæ.

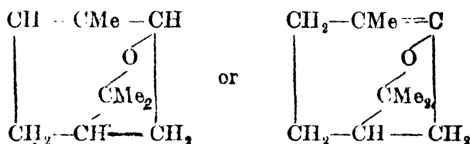


Pinene — Intermediate Product — Pinene hydrochloride

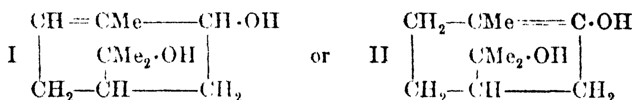
The presence of a double bond in the pinene molecule is indicated by the formation of **dibromides,** an oil and a solid melting at 169°, and also by the formation of a glycol, **pinene glycol,** $C_{10}H_{16}(OH)_2$, by the action of dilute permanganate.

The constitution of pinene is based largely upon that of **pinole,** $C_{10}H_{16}O$, a product obtained by the elimination of water from **soberol,** $C_{10}H_{16}(OH)_2$, which is formed when pinene is left exposed to sunlight in contact with air and water. With dilute permanganate, pinole, which is an unsaturated ether, yields **pinoleglycol,** $C_{10}H_{16}O(OH)_2$, and this on further oxidation yields a tetrahydric alcohol, **sobrerythritol,** $C_{10}H_{16}(OH)_4$,

which can be oxidized to terpenylic acid. Pinole presumably contains the same grouping of carbon atoms as terpenylic acid (see p. 624), and should be either:



Sobrerol would then be:



but since sobrerol on further oxidation yields a tetrahydric alcohol and not a trihydroxy-ketone, formula I with a CH(OH) group is correct, and the formula on p. 627 follows for pinene (*Wagner*).

When boiled with dilute acids pinene yields terpineol or its esters; such a transformation is explicable if the assumption is made that the four-membered ring is unstable, and that a rupture between the CMe_2 and upper CH-group occurs. A similar rupture, accompanied by the wandering of a chlorine atom, occurs in the transformation of pinene nitroso-chloride into hydrochlorocarvoxime under the influence of hydrochloric acid.

When pinene is oxidized with permanganate the double linking is broken and a monobasic ketonic acid, α-**pinonic acid,**

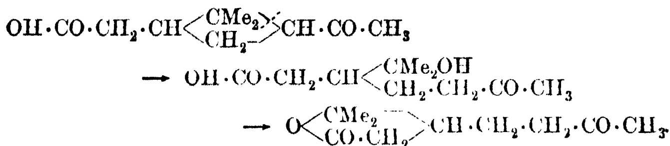


is formed, and this on further oxidation yields the dibasic acid **pinic acid,**



from which **norpinic acid,** 1:1-*dimethyl-cyclobutane*-2:4-*dicarboxylic acid,* can be obtained (*Baeyer*, B. **29,** 1907), indicating that the four-membered ring is stable in the presence of oxidizing agents, although readily ruptured by hydrolysing

agents, *e.g.* pinonic acid yields when hydrolysed a lactone, homoterpenylic methyl ketone (cf. p. 624).

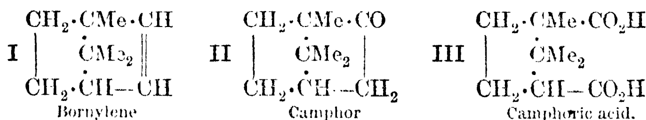


The only reactions of pinene difficult to account for by means of *Wagner's* formula are its oxidation to isoketocamphoric acid, isocamphoronic acid, and terebic acid (*Tiemann* and *Semmler*, B. **29**, 529, 3027; *Perkin*, Proc. 1900, 214).

The isomeric β-pinene (**nopinene**) occurs in many turpentines, *e.g.* French oil, 37 per cent. It is characterized by the readiness with which it is oxidized to nopinone ($C:CH_2$ replaced by $C:O$). Its structure as α-pinene, in which the olefine linking in the ring has become replaced by a semi-cyclic olefine linking between carbons 1 and 7, follows from its synthesis from nopinone and ethyl bromoacetate (cf. β-phellandrene, p. 622).

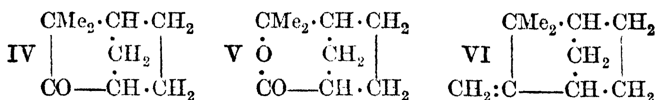
Bornylene is obtained by the action of alkalis on bornyl iodide (from pinene and hydrogen iodide), and as it is readily oxidized to camphoric acid it is represented by formula I.

The corresponding saturated hydrocarbon **camphane,** $C_{10}H_{18}$, the parent substance of the camphor group, is obtained by reducing bornyl iodide. It melts at 154°, and is optically inactive; its molecule should therefore be symmetrical.



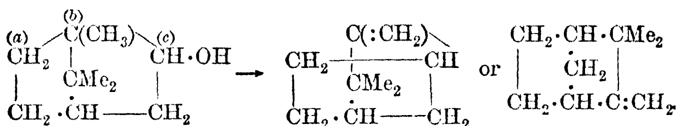
Camphene, *d* and *l*, is a solid, m.-pt. 50°. It can be obtained from pinene by combining with hydrogen chloride, forming bornyl chloride, and then removing hydrogen chloride by means of alkalis. For some years it was represented by formula I, but it does not yield camphoric acid when oxidized. *Harries* and *Palmen* (B. 1910, **43**, 1432) have shown that it forms an ozonide when its acetic-acid solution is saturated with ozone, and that this when warmed yields a mixture of

camphenilone (30 per cent) (IV), and *d*-hydroxy-camphenilic



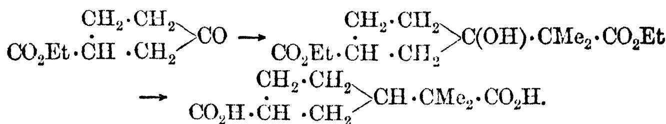
acid lactone (50 per cent) (V), and they therefore favour *Wagner's* formula VI for camphene.

The formation of camphene from bornyl chloride must involve rearrangements within the molecule. *Meerwein* (A. 1914, **405**, 129) represents the change as follows:—



The change thus consists in a fission between C atoms *a* and *b*, and subsequent union between C atom *a* and the C atom *c* to which the OH group of borneol was attached.

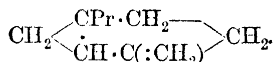
The molecular refraction (*Auwers*, A. 1912, **387**, 240) agrees with *Wagner's* formula. Its oxidation products are (*a*) camphenilone (oxidation of $C:CH_2$ to CO), (*b*) with alkaline permanganate camphenic acid, (*c*) with nitric acid, camphoric acid, and finally 2:2-dimethylcyclopentane-1:1:3-tricarboxylic acid. **Camphenic** acid, 3-carboxy-cyclopentane-1-iso-butyric acid, has been synthesised by *Lipp* (B. 1914, **47**, 871) from ethyl cyclopentane-1-one-3-carboxylate and ethyl α-bromoisobutyrate in the presence of zinc; then eliminating water from the hydroxy ester, and reducing the resulting unsaturated ester with hydrogen and platinum black.



The reactions of camphene and bornylene with ethyl diazoacetate confirm the formulæ I and VI. The normal reaction with unsaturated compound is for nitrogen to be eliminated and the formation of a cyclopropane ring between the C atom

of the CH_2 group of the diazo ester, and the two C atoms united by the olefine linking. Camphene, if represented by formula VI, should thus give a compound containing the grouping, $\begin{matrix} CH_2\cdot C< \\ \diagdown\ \diagup \\ CH\cdot CO_2H \end{matrix}$, and this on final oxidation should yield cyclopropane-1:1:2-tricarboxylic acid, whereas if it has the structure represented by formula I, originally attributed to camphene but now assigned to bornylene, it should yield as final oxidation product cyclopropane-1:2:3-tricarboxylic acid. In reality it has been found that camphene gives the 1:1:2-tricarboxylic acid and bornylene the isomeric 1:2:3-acid. (*Büchner* and *Weigand*, B. 1913, **46**, 759, 2108.)

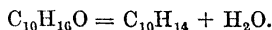
Sabinene occurs in marjoram oil; it has b.-pt. 163°–165° and $[\alpha]_D$ + 80°. It forms a hydrochloride and a nitroso-chloride; when oxidized it yields a ketone by the replacement of CH_2 by O, and therefore probably contains a methylene group attached to the nucleus. It also probably contains a three-membered ring and is represented as



The tri-ring is readily ruptured, as sabinene and its derivatives can be transformed into terpinene and related hydroxy compounds. α and β Thujenes, $C_{10}H_{16}$ (*Tschugaeff*, B. **34**, 2279; **37**, 1481), also contain a tri-ring and a double linking in positions 1 and 3 respectively.

II. **Camphors.**—The most important variety is:

Common or **Japan camphor,** $C_{10}H_{16}O$, which is found in the camphor tree (*Laurus camphora*), and can be obtained from the latter by distillation in steam. It forms colourless, transparent, glistening prisms of characteristic odour. It melts at 175°, boils at 204°, has a sp. gr. 0·985, and can be sublimed readily. It is dextro-rotatory in alcoholic solution, the amount of rotation varying with the source of the camphor. When distilled with phosphoric anhydride it yields cymene; zinc chloride at high temperatures also transforms camphor into cymene, though in the latter case the reaction is less simple:

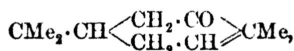


$$C_{10}H_{16}O = C_{10}H_{14} + H_2O.$$

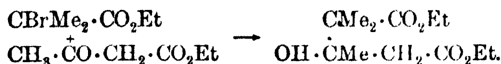
When heated with iodine it yields carvacrol, *i.e.* hydroxy-

cymene (p. 446), just as oil of turpentine yields cymene. Nitric acid oxidizes it to the dibasic **camphoric acid,** $C_8H_{14}(CO_2H)_2$, which somewhat resembles phthalic acid (see B. **23,** 218), and then to **camphoronic acid,** unsym. trimethyl-carballylic acid, &c. Camphor reacts with hydroxylamine to produce **camphor-oxime,** $C_{10}H_{16}(NOH)$, and therefore contains a carbonyl group, and with nitrous acid to produce **isonitroso-camphor,** $C_{10}H_{14}O:N\cdot OH$, and thus contains the group $\cdot CH_2\cdot CO$. The oxime by the loss of water is converted into the **cyanide,** $C_9H_{15}\cdot CN$, which yields **campholenic acid,** $C_9H_{15}\cdot CO_2H$, on saponification, and **camphylamine,** $C_9H_{15}(CH_2\cdot NH_2)$, on reduction (B. **21,** 1125).

A considerable amount of attention has been devoted by various chemists to the question of the constitution of camphor) *Lapworth,* B. A. Report, 1900, 299). At first, great importance was attached to the readiness with which camphor can be transformed into benzene derivatives, *e.g.* cymene and carvacrol, and attempts were made to represent it as a simple six-carbon ring compound, *e.g. Kekulé.*

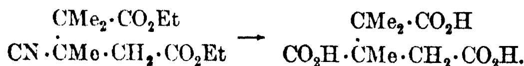


whereas others represented it as a bridged six-carbon ring. In 1893 *Bredt* suggested the formula II (p. 629), which is now generally accepted, and which has been confirmed recently by the synthesis of camphoric acid. *Bredt* drew especial attention to the oxidation products of camphor, namely camphoric, camphoronic, and trimethyl-succinic acid previously obtained by *Koenigs.* He showed that camphoronic acid when heated gave trimethyl-succinic, isobutyric, and carbonic acids and carbon, and suggested the formula $CO_2H\cdot CH_2\cdot CMe(CO_2H)\cdot CMe_2\cdot CO_2H$, viz. α-α-β-trimethyl-carballylic acid, a constitution which has since been confirmed by *W. H. Perkin* and *Thorpe's* synthesis (J. C. S. 1897, 1169). This consists in condensing ethyl acetoacetate and ethyl α-bromo-isobutyrate by means of zinc to ethyl β-hydroxy-α-α-β-trimethyl glutarate:

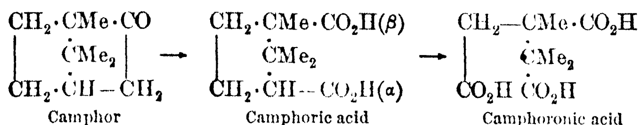


The OH group is replaced by Cl, and this by CN, and

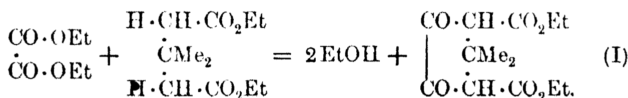
the cyano-ester when hydrolysed yields camphoronic acid:



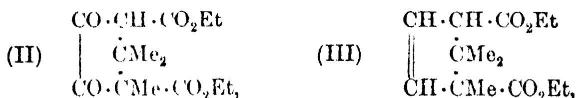
The relationship between camphor and its oxidation products is thus simple, as shown by the following scheme:—



Camphoric acid has been synthesised by *Komppa* (B. 1901, **34**, 2472; 1903, **36**, 4332; J. C. S. 1911, **99**, 2010). Ethyl oxalate and ethyl ββ-dimethyl-glutarate condense in the presence of sodium ethoxide, yielding diketo-apocamphorate I:



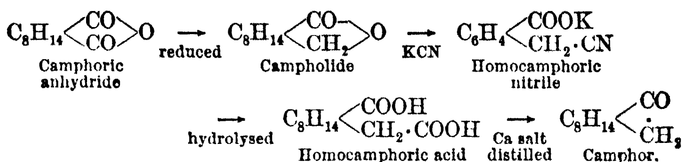
which, methylated by means of sodium and methyl iodide, yields the ethyl ester of diketo-camphoric acid II:



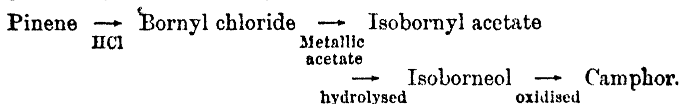
and this can be reduced with sodium amalgam to dihydroxy-camphoric acid; further reduction with phosphorus and hydriodic gives dehydro-camphoric acid, III, which combines with hydrogen bromide; and the β-bromo-camphoric acid thus obtained, when reduced with zinc and acetic acid, yields the racemic modification of camphoric acid.

A synthesis from $CMe_2<\begin{matrix}CH(CO_2H)\cdot CH_2\\ CH(CO_2H)\cdot CO\end{matrix}$, has been accomplished by somewhat similar steps.

Camphor can be synthesised from camphoric acid by the following series of reactions (*Haller*, C. R. 1896, **122**, 446):



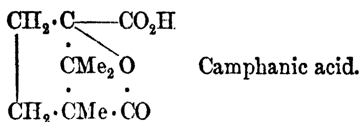
Considerable amounts of camphor are manufactured from pinene by the following series of reactions:



(Cf. *Housemann*, Sci. Progress, 1908, **3**, 60.)

Camphoric acid is an unsymmetrical dibasic acid, as it gives two isomeric monomethyl esters and two amic acids. One carboxylic acid is probably attached to a tertiary and the other to a secondary carbon atom, as the acid yields a single *mono*bromo substituted derivative when subjected to the *Hell-Volhard-Zelinsky* method of bromination. The derivatives are known respectively as α and β (or ortho and allo), the α-methyl ester, for example, contains the group $>CH \cdot CO_2Me$, and the β-methyl ester the group $\geqslant C \cdot CO_2Me$. As isonitroso-camphor—$C(:NOH) \cdot CO$—when warmed with hydrochloric acid yields α-camphoramic acid, $>CH \cdot CO \cdot NH_2$, it follows that the methylene group of camphor corresponds with the α-carboxylic group in camphoric acid.

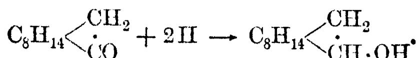
Camphoric acid exists in four optically active and two racemic modifications, the latter known respectively as *r*-camphoric and *r*-isocamphoric acids. This points to the presence of two asymmetric carbon atoms in the molecule of the acid, as indicated in the formula. Camphor, on the other hand, exists in two active and one racemic form only. When *d*-camphoric acid is racemized the product is not *r*-camphoric acid, but a mixture of the original acid with *l*-iso-camphoric acid. This is due to the fact that only one asymmetric carbon atom is concerned in the racemization. In the oxidation of camphoric acid to camphoronic acid, **camphanic acid,** the lactone of α-hydroxy-camphoric acid is formed as an intermediate product; its constitution follows from the fact that it is formed by boiling bromo-camphoric anhydride with water.



Various **chloro-**, **bromo-**, **nitro-** and **amino-camphors** are known. The mono-substituted derivatives, $C_8H_{14}\langle{CHX \atop CO}$, exist in two stereoisomeric forms.

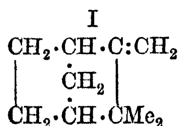
For β camphor, the compound in which the CH_2 and CO groups of the >CMe·CO·CH_2·CH< chain are reversed, *i.e.* >CMe·CH_2·CO·CH<, see *Bredt* and *Perkin*, P. 1912, **28**, 56.

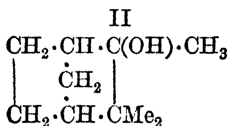
Borneol or **Borneo camphor,** $C_{10}H_{17}$·OH, occurs in nature (in *Dryobalanops camphora*), and is produced by the action of nascent hydrogen upon Japan camphor:

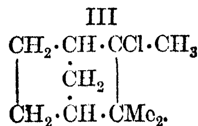


It resembles the latter, but has at the same time an odour of pepper. It crystallizes in hexagonal plates, melts at 208°. boils at 212°, and when oxidized yields in the first instance camphor. Borneol possesses the character of a secondary alcohol, yielding esters, and with PCl_5 yields **bornyl chloride**, $C_{10}H_{17}Cl$ (m.-pt. 148°), which is identical with pinene hydrochloride, together with large amounts of isobornyl chloride. With HI, on the other hand, it yields bornyl iodide and no iso-compound.

Isoborneol is formed, together with larger quantities of borneol, by reducing camphor with sodium and alcohol, and was for a long time regarded as stereoisomeric with borneol; but the readiness with which its chloride yields camphene, and the readiness with which it combines with organic acids in the presence of sulphuric acid to form esters of isoborneol, indicate a close relationship between camphene (I) and isoborneol, and the formula II has been accepted. III represents isobornyl chloride:

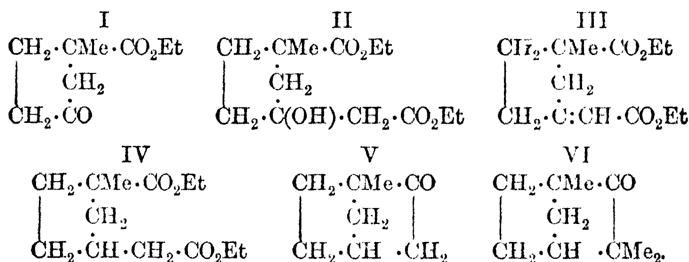




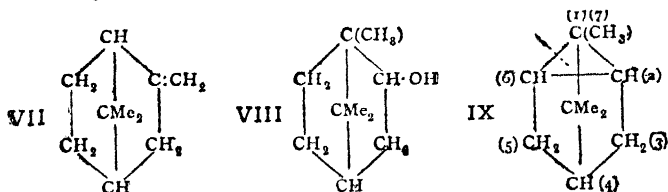


The formation of isobornyl chloride from borneol and PCl_5 is to be attributed to the dehydration of borneol to camphene and the addition of HCl to the latter. Isoborneol melts at 212°, is very volatile, and when oxidized yields camphor.

Fenchone, α-methylcamphenilone, which is isomeric with camphor, occurs in fennel oil, is represented by *Semmler* (A. 1912, **387,** 1) by formula VI (below), and its complete synthesis has been achieved (*Ruzicka,* B. 1917, **50,** 1362). Ethyl 1-methylcyclopentane-3-one-1-carboxylate (I), ethyl bromoacetate and zinc yield ethyl 3-hydroxy-3-carbethoxymethyl-1-methylcyclopentan-1-carboxylate (II), which reacts with PBr_3, yielding the unsaturated ester, ethyl dehydromethylnorhomofenchonate (III), which is readily reduced to ethyl methylnorhomocamphorate (IV), and the lead salt of this heated in a current of CO_2 yields methylnorcamphor (V), which with methyl iodide and sodamide gives a mixture of fenchone (VI) and fenchosantanone (the monomethyl derivative):



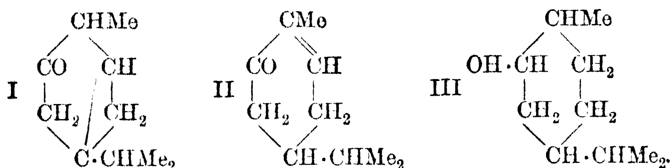
Fenchenes.—The hydrocarbons known as fenchenes appear to have a ring system different from that of fenchone, *e.g.* α-fenchene, obtained by dehydrating fenchyl alcohol, is represented by formula VII:



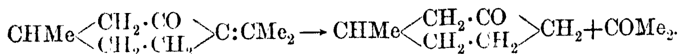
The change in ring structure from fenchyl alcohol to α-fenchene

is thus the reverse of that met with in the conversion of borneol into camphene (p. 629), and the simplest explanation in each case is the formation of a tricyclic system, *e.g.* in the case of borneol (VIII), of the product IX, and then by subsequent fission of the cyclopropane ring at the position indicated, and the wandering of one H atom from C atom (7) to C atom (6). (*Ruzicka*, Helv. 1918, **1**, 110). Hydrocarbons corresponding with this intermediate product have been isolated by *Bredt* by condensing camphor or fenchone with *Grignard* reagents, and eliminating water from the tertiary alcohols so obtained. Using magnesium methyl iodide, a hydrocarbon with methyl in position 2 in formula IX is obtained, and similar phenyl and naphthyl derivatives have been prepared (J. pr. 1918, **98**, 96).

Thujone (I) occurs in thuja, wormwood, and sage oils; it is not unsaturated, and hence contains a bicyclic system; when heated it forms carvotanacetone (II), and this is readily reduced to carvomenthol (III):

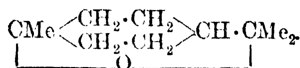


Pulegone, $C_{10}H_{16}O$, occurs in oil of pennyroyal and is represented as a monocyclic ketone with the ketonic group in position 3, and a semicyclic olefine bond in position 4:8. This structure follows from the readiness with which it is oxidized to β-methyladipic acid and also to the fact that when heated with formic acid at 250° it yields acetone and 1-methylcyclohexane-3-one:



Cineol, or eucalyptol, $C_{10}H_{18}O$, occurs in cardamom, cajuput, eucalyptus, and wormseed oils, and is also formed by treating terpin (p. 625) with acids. It boils at 176°–177°, is optically inactive, and forms characteristic hydrochloride, phosphate, and arsenate, which are utilized in its estimation. It also

forms additive compounds with phenols. It has no alcoholic or ketonic properties, and is usually represented as an internal anhydride or ether of terpin, viz.:

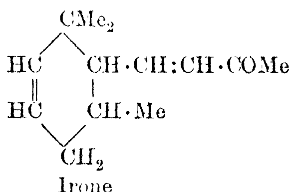


A very convenient method for converting terpene aldehydes or ketones into the corresponding hydrocarbons ($CO \rightarrow CH_2$) is by heating their semicarbazones or hydrazones at 160°–200° with a little sodium ethoxide: $> C{:}N{\cdot}NH_2 \rightarrow > CH_2 + N_2$. Treated in this way camphor gives a nearly quantitative yield of camphane.

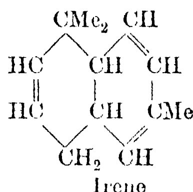
D. Compounds related to Terpenes

Irone—a methyl ketone, $C_{13}H_{20}O$—is the odoriferous principle of the iris root, and also probably of the violet. When boiled with hydriodic acid it yields the hydrocarbon **irene,** $C_{13}H_{18}$.

The formulæ suggested by *Tiemann* and *Krüger* are:



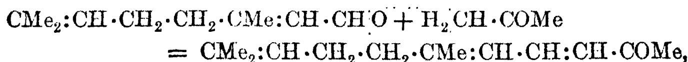
Irone



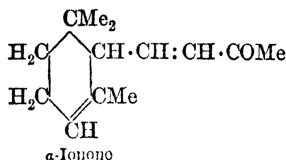
Irene

(cf. B. 26, 2675). These chemists have synthesised two isomerides of irone, which they term α- and β-**ionones.** These also possess the odour of violets, and are employed at the present time for the manufacture of violet essence.

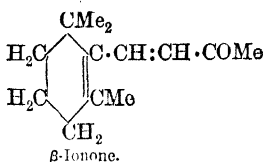
The synthesis consists in the condensation of citral (p. 613) with acetone to form the unsaturated ketone pseudo-ionone:



which is transformed into the ring compounds α- and β-ionones when boiled with sulphuric acid:

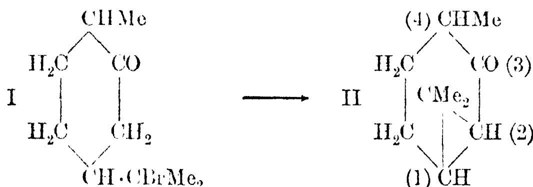


α-Ionone

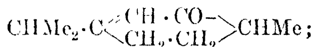


β-Ionone.

Carone, $C_{10}H_{16}O$ (II), is one of the most important ring ketones of the terpene series, and is formed when dihydrocarvone hydrobromide, 8-bromoterpane-2-one (I), is treated with alcoholic potash (*Baeyer*, B. 1896, **29**, 5 and 2796).



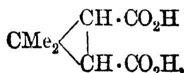
It is a colourless oil with an odour of camphor and peppermint, and boils at 210°, but is, at the same time, partially transformed into the isomeric carvenone. The molecule, according to *Baeyer*, contains a six-carbon ring with a bridge. One of the most characteristic properties is the readiness with which the bridge is broken and derivatives of *p*- or *m*-terpane are produced. Thus when heated it yields carvenone or Δ-3-*p*-terpene-2-one,



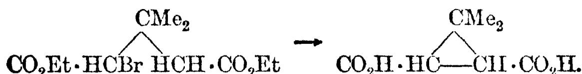
with hydrobromic acid it yields 8-bromoterpane-2-one, and with sulphuric acid 8-hydroxy-terpane-2-one,



When oxidized, carone yields a dibasic acid, **caronic acid,** (*cis* and *trans* modifications), which *Baeyer* suggested was 1:1-dimethyl-cyclopropane-2:3-dicarboxylic acid,



a conclusion which has been confirmed by *Perkin's* synthesis (J. C. S. 1899, 48) from ethyl dimethylacrylate, $CMe_2:CH\cdot CO_2Et$, and ethyl sodio-malonate (or ethyl sodio-cyanoacetate). The product, ethyl dimethylpropane-tricarboxylate, $(CO_2Et)_2CH\cdot CMe_2\cdot CH_2\cdot CO_2Et$, when hydrolysed and heated at 200°, yields ββ-dimethyl-glutaric acid, $CO_2H\cdot CH_2\cdot CMe_3\cdot CH_2\cdot CO_2H$. The α-bromo-derivative of the ethyl ester of this acid, $CO_2Et\cdot CHBr\cdot CMe_2\cdot CH_2\cdot CO_2Et$, yields *cis* and *trans* caronic acids when heated with alcoholic potash:



The hydrocarbons Δ³- and Δ⁴-**carenes**,* $C_{10}H_{16}$, have been isolated by *Simonsen*; the former from *Pinus longifolia* (J. C. S. 1920, 571), and the latter from the oil of *Andropogon Jwarancusa* (1922, 2294); on oxidation both yield compounds containing the cyclopropane ring, the former giving caronic acid and the latter 1:1-dimethyl-2-γ-ketobutylcyclopropane-3-carboxylic acid. On the other hand the cyclopropane ring is readily ruptured by acids and both hydrocarbons react with hydrochloric acid yielding mixtures of the hydrochlorides of dipentene and sylvestrene. The sylvestrene obtained from certain natural products apparently does not exist as such in the original material, but is formed from the carenes present by the method of treatment with hydrochloric acid. It is thus probable that derivatives of *m*-terpane do not occur in nature, but are products of intra-molecular change (J. C. S. 1925, 2494).

With compounds containing a di- or tri-cyclic system, it must be remembered that in most cases the different rings do not lie in the same plane. This is most readily seen with the aid of models, and holds good for camphor, camphene, fenchone. The usual single plane formulæ, therefore, do not represent the actual spatial relationships of the group.

In a survey of the bi-cyclic systems attention should be drawn to the stability of tri- and tetra- rings systems to oxidizing agents and their instability towards hydrolysing agents. By means of these reagents it is frequently possible to arrive at valuable information concerning the structure of a given di-cyclic compound. By the aid of oxidizing agents

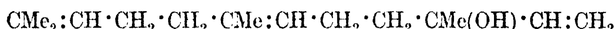
* See Carone formula, p. 639, for numbering.

simple derivatives of cyclopropane or cyclobutane can be formed, and by the aid of hydrolysing agents derivatives of cyclohexane.

E. Sesquiterpenes and related Oxygen Compounds

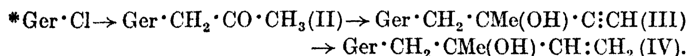
A detailed study of these compounds has been made within recent years, especially by *Ruzicka*, and the results published in Helv. 1921–1930. Like the terpenes proper they may be divided into: (*a*) open chain compounds with four olefine linkings; (*b*) monocyclic systems with three; (*c*) dicyclic with two, and (3) tricyclic with only one olefine linking. A clue as to which of these groups a given compound belongs can be obtained by a study of the number of hydrogen atoms it can take up when catalytically reduced and also from a study of its molecular refraction as for a hydrocarbon, $C_{15}H_{24}$, the values vary from 69·6 for an open chain compound to 64·4 for a tricyclic system. Attention must, however, be paid to the exaltation of the refractive produced by conjugate double bonds and by semicyclic bonds (Chap. XLVII, D).

1. *Open chain compounds.*—**Nerolidol**, $C_{15}H_{25}\cdot OH$, occurs in orange flowers and Peru bark, and its structure as 2:6:10-trimethyl-$\Delta^{2:6:11}$dodekatriene-10-ol,



$$CMe_2{:}CH\cdot CH_2\cdot CH_2\cdot CMe{:}CH\cdot CH_2\cdot CH_2\cdot CMe(OH)\cdot CH{:}CH_2$$

has been established by its synthesis from genanyl chloride, which reacts with ethyl acetoacetate yielding dihydropseudo-ionone (II) and this condensed with acetylene in presence of sodamide yielding dehydronerolidol (III) which can be reduced by sodium and moist ether to nerolidol (IV).



$$^{*}Ger\cdot Cl \rightarrow Ger\cdot CH_2\cdot CO\cdot CH_3(II) \rightarrow Ger\cdot CH_2\cdot CMe(OH)\cdot C{:}CH(III) \rightarrow Ger\cdot CH_2\cdot CMe(OH)\cdot CH{:}CH_2\,(IV).$$

Closely allied to and isomeric with nerolidol is **farnesol**, obtained from the flowers of *Acacia farnesiana* and other species of Acacia. The fact that treatment with acetic anhydride converts it into nerolidol (together with some **farnesene**), just as linalool is converted into nerol, suggests that it bears the same relationship to nerolidol that linalool does to nerol,

*** Ger stands for the geranyl group $CMe_2{:}CH\cdot CH_2\cdot CH_2\cdot CMe{:}CH\cdot CH_2$.**

and is therefore Ger·CH_2·CMe:CH·CH_2·OH, and this structure is confirmed by the fact that it is readily oxidized to the corresponding aldehyde, **farnesal,** and the oxime of this when dehydrated yields a nitrile which on hydrolysis gives dihydropseudoionone (O and H_2 adding on to olefine linking and producing fission).

2. **Monocyclic sesquiterpenes and alcohols.**—α-Bisabolol obtained as its acetate from farnesene by treatment with acetic and sulphuric acids, yields a trihydrochloride, m.-pt. 79°, identical with that from natural bisabolene from oil of opopanea (1925, 259), and the alcohol is represented as Δ^1-tetrahydrotoluene with a ·CMe(OH)·CH_2·CH_2·CH:CMe_2 group in position 4, ring closure having taken place under the influence of the acids.

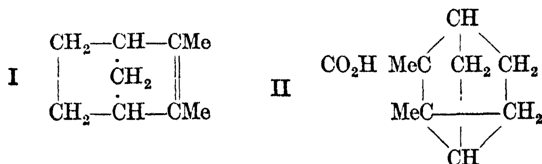
3. **Dicyclic sesquiterpenes.**—These have been studied in great detail and most of them contain a reduced naphthalene skeleton. The presence of this skeleton in **cadinene** from oil of cubebs, cade oil and juniper wood, was rendered highly probable when *Ruzicka* (1921, 505; 1922, 369) obtained **cadalene** by heating cadinene with sulphur and so removing hydrogen sulphide (*Vesterberg's* method), and then by synthesis proved cadalene to be 1:7-dimethyl-4-isopropylnaphthalene. The starting-point in this synthesis is *p*-cymyl-2-acetic acid (1-methyl-4-isopropyl-2-acetic acid) C_3H_7·C_6H_3Me·CH_2·CO_2H; when reduced by *Bouveault's* method it yields the corresponding primary alcohol ·CH_2·CH_2·OH, the bromide of which condenses with sodio-methylmalonic ester yielding ·CH_2·CH_2·CMe $(CO_2Et)_2$, and from this by hydrolysis and elimination of carbon dioxide the monobasic acid, ·CH_2·CH_2·CHMe·CO_2H, is formed. The chloride of this acid with aluminium chloride (*Friedel-Craft's* reaction) undergoes internal condensation, the second ring is formed and the product, 1:7-dimethyl-4-isopropylnaphthalene, is identical with cadalene. The only point in dispute at present are the positions of the olefine linkings in cadinene. These are undoubtedly in the rings and not in side chains, and according to *Ruzicka* and *Stoll* (1924, 94) ordinary cadinene is probably a mixture of the $\Delta^{3:6}$- and $\Delta^{3:7}$- 1:7-dimethyl-4-isopropylhexahydronaphthalene (see also *Henderson* and *Robertson*, J. C. S. 1926, 2811).

Eudesmol, $C_{15}H_{25}$·OH, from Eucalyptus oil and **selinene,** $C_{15}H_{24}$, from celery-seed oil, when heated with sulphur according to *Vesterberg's* method, yield not only hydrogen sulphide,

but also methyl sulphide, by the loss of one of the original methyl groups, and the other product is 6-methyl-4-isopropylnaphthalene (eudalene), the structure of which again has been proved by direct synthesis. The methyl group removed by the action of sulphur is undoubtedly one attached to carbon atom No. 5 or No. 10 of the naphthalene ring, i.e. the two carbon atoms common to the two benzene nuclei; the 5 position is more probable as this readily admits of the formation of 1 molecule of selinene from 3 of isoprene. The formula given by *Ruzicka* and *Capato* for eudesmol is 1-methylene-5-methyl-8-isopropyl-8-hydroxy-dekahydronaphthalene (A. 1927, **453,** 62). The presence of the methylene group is proved by the formation of a ketonic group CO in position 1 after ozonolysis, and position 8 for the hydroxyl group is selected since dihydroeudesmol (2H added to semicyclic linkage) on ozonolysis yields a ketone with CO in position 8.

Zingiberene, $C_{15}H_{24}$, obtained from oil of ginger, contains 3 olefine linkings, as it can take up 6 atoms of hydrogen by catalytic reduction, and should therefore be a monocyclic compound, and its relatively high molecular refraction can be accounted for if two of the three linkings are conjugate. Treated with hydrogen chloride it yields the dihydrochloride of isozingiberene from which **isozingiberene** can be isolated by treatment with alkali. Both the hydrocarbons yield cadalene when heated with sulphur. Zingiberene is probably 1-methyl-4-propenylcyclohexane with a $\cdot CH:CH\cdot CMe:CH_2$ group in position 2 or 3, and isozingibere 1:7-dimethyl-4-propenyloctahydronaphthalene (1922, 359).

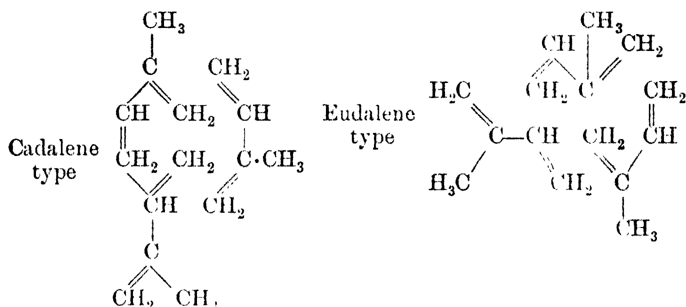
East Indian Sandalwood oil contains many constituents, but mainly α- and β-santalols, $C_{15}H_{24}O$, together with santene, C_9H_{16}, teresantalol, $C_{10}H_{16}O$, and santalene, $C_{15}H_{24}$. Santene, as a result of its synthesis (Bull. Soc. 1917, **21,** 13), has been shown to be 2:3-dimethyl-Δ^2-cyclohexene with a methylene bridge in the position 1:4 (Formula 1):



Teresantalic acid differs from santene by CO_2; it is a monobasic

acid with no unsaturated characteristics, and its properties are in harmony with the view that it contains a cyclopropane ring in place of the cyclic ethylene linking in santene and thus has the structure given in Formula II (cf. Cage systems, Chap. LII). α-Santalol from which teresantalic acid is formed by oxidation probably has the $\cdot CH_2 \cdot CH:CMe \cdot CH_2 \cdot OH$ group in place of the carboxylic group.

The structural formulæ for most of the terpenes and sesquiterpenes, whether of the open chain, monocyclic or dicyclic types, are in complete harmony with the view that these compounds are polymerised isoprene, e.g.



It has been suggested that **squalene,** a hydrocarbon present in large quantities in the unsaponifiable fraction of certain fish oils is a dihydrotriterpene $C_{30}H_{50}$ (*Heilbron*, J. C. S. 1928, 942; 1929, 873).

XLII. RESINS; OLEORESINS; GLUCOSIDES

A. Resins

Many organic compounds, the terpenes in particular, possess the property of becoming " resinified " by oxidation in the air or under the influence of chemical reagents, *i.e.* of being converted into substances very similar to the resins which occur in nature. These natural resins are solid, amorphous, and generally vitreous brittle masses of conchoidal fracture, insoluble in water and acids, but soluble in alcohol, ether, and oil of turpentine. They are found naturally in abundance, partly also as balsams or oleoresins, *i.e.* dissolved in terpenes or ethereal oils, from which they can be separated by distilling in steam. The resins dissolve in alkalis to form compounds of the nature of soap (resin soaps), being again precipitated from the aqueous solutions of these on the addition of acids; most resins must therefore consist of a mixture of somewhat complicated acids (the so-called resin-acids), or frequently their anhydrides.

Abietic acid, $C_{19}H_{28}O_2$, has been isolated from rosin or colophonium (the residue from the distillation of turpentine); it crystallizes in small plates, melts at 153°, and is soluble in hot alcohol. It probably contains a retene (p. 544) skeleton as this hydrocarbon is formed on dehydrogenation with sulphur. (*Ruzicka*, Helv. 1923, 1077, 1097; 1925, 632, 637; cf. *Aschan*, *Levy* and *Brunotte*, B. 1927, 1923). **Pimaric acid,** $C_{20}H_{30}O_2$, has been prepared from galipot resin (*Pinus maritima*), and from French and American rosin (*Knecht* and *Hibbert*, J. S. Dyers, 1919, 35, 148). It melts at 144°–146°, and closely resembles abietic acid.

The resins show their relation to the aromatic compounds by their conversion into hydrocarbons of the benzene or naphthalene series when distilled with zinc dust, and by the formation of di- and trihydroxy-benzenes when they are fused with potash.

An important resin is **shellac,** manufactured from East Indian lac, the exudation of an organism known as the lac insect (*Tachardia lacca*), which grows on certain species of jungle trees. It is a constituent of all high-grade varnishes. **Amber** is a fossil resin which contains succinic acid in addition

to resin-acids and a volatile oil. Other resins are:—**copal,** of which there are numerous varieties, *e.g.* Zanzibar, which contains 80 per cent of *trachylolic acid*, $OH \cdot C_{54}H_{85}O_3 \cdot COOH$; **dammar** of South India; **dragon's blood,** containing esters of the alcohol **drachoresotannol,** $C_8H_9O \cdot OH$.

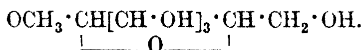
Among important oleoresins are **Storax** from *Liquid amber orientalis*, containing cinnamene derivatives (p. 484), **Balsam of Tolu** (*Myroxylon toluifera*) and **Balsam of Peru** (*M. pereiræ*) containing esters of benzoic and cinnamic acids, and **Copaiba balsam** containing sesquiterpenes.

The resins are largely used for the manufacture of lacs, varnishes, &c.

B. Glucosides

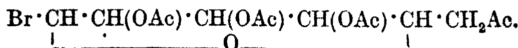
Glucoside is the name given to a number of complex organic compounds which occur in vegetable tissues. They are all characterized by the fact that on hydrolysis with acids, alkalis, or enzymes, a sugar—usually *d*-glucose—is formed. They are therefore to be regarded as anhydro-compounds of *d*-glucose or some other sugar with various organic compounds.

In addition to these natural glucosides, the constitutions of many of which are unknown, *E. Fischer* has prepared artificially glucosides of the type of α- and β-methyl-glucosides (p. 322) by the action of methyl alcohol and hydrogen chloride on glucose (cf. J. C. S. 1929, 300. These are stereoisomeric compounds:



The α-compound melts at 165° and the β- at 107°. The optical rotatory powers are respectively +157° and −33°. They do not reduce *Fehling's* solution, and on hydrolysis yield *d*-glucose and methyl alcohol. For further details of the isomerism, see Chapter XLVIII, B, Enzyme action. The compound termed **glucosimine,** and prepared by the action of a methyl alcoholic solution of ammonia on glucose, is methyl-glucoside, in which the CH_3 group is replaced by NH_2 (*Levene*, J. Biol. C. 1916, **24,** 59).

More complex glucosides have been synthesised by *Fischer* and others by means of acetobromoglucose,



a compound first prepared by *Fischer* and *E. F. Armstrong* (B. 1901, 2885) by the action of hydrobromic acid in acetic acid on penta-acetylglucose. Other monosaccharoses yield similar derivatives, and these bromine compounds have been used for the synthesis of various types of glucosides, galactosides, &c. They condense with ethereal solutions of various alcohols, yielding acetylated glucosides analogous to the acetylated methyl glucosides, and on careful hydrolysis the glucosides themselves are formed. (*Fischer*, B, 1910, 2521; 1912, 2467; 1914, 1377, J. C. S. 1929, 1676. For phenolic glucosides cf. B. 1916, 2813; 1917, 711; cholesterol glucosides, *Salway*, J. C. S. 1913, 41; gallic acid glucosides, *Fischer* and *Strauss*, B. 1912, 3773; galactosides, J. C. S. 1929, 1820.) Mustard oil glucosides are formed by condensing the bromo-compounds with the silver salts of thiourethanes, R·N:C(OEt)·SAg (B. 1914, 1258); and purin glucosides (B. ibid. 210, 1377) from the silver salts of purins. The purin compounds, *e.g.* theophyllene-glucoside, condense with phosphoryl chloride, yielding the acid, $C_{13}H_{16}O_7N_4 \cdot PO_2H$, $2H_2O$, which may be regarded as the first step in the synthesis of nucleic acids (p. 658). For terpene glucosides cf. *Hämäläinen*, Abs. 1913, i., 497, 639, and for alkaloid glucosides *Mannich*, A. 1912, **394**, 233; *Irvine* and *Hynd*, J. C. S. 1913, 41.

Among the commoner natural glucosides are:

Amygdalin, $C_{20}H_{27}O_{11}N$ (p. 452), found in bitter almonds, in the leaves of the cherry laurel, in the kernels of the peach, cherry, and other Amygdalaceæ. It crystallizes in colourless prisms, melts at 200°, is readily soluble in water, and on hydrolysis with emulsin yields benzaldehyde, *d*-glucose, and hydrogen cyanide. Emulsin is an enzyme which occurs in bitter almonds. It is characteristic of most glucosides that in the plant tissue they are accompanied by an enzyme, which is able in the presence of water to hydrolyse them. Amygdalin may also be hydrolysed by dilute mineral acids.

With concentrated hydrochloric acid it yields *l*-mandelic acid, and with an enzyme contained in yeast (amygdalase) it yields glucose and *l*-mandelonitrile-glucoside. A synthetic *dl*-mandelonitrile-glucoside has been synthesised by the following stages:—condensing acetobromoglucose with *dl*-ethyl mandelate, converting the product into the corresponding amide, removal of the acetyl groups by hydrolysis, and elimination of water from the amide by means of $POCl_3$.

Isoamygdalin, obtained by the action of alkalis on amygdalin, is the racemic form of which ordinary amygdalin is the *l*-modification. Amygdalin is the commonest of the *cyanogenetic glucosides, i.e.* glucosides which give rise to hydrogen cyanide in plant tissues or on hydrolysis. Some of the other members are: **dhurrin,** *p*-hydroxy-mandelonitrile-glucoside (*Dunstan* and *Henry*), in the great millet; **phaseolunatin,** acetone-cyanohydrine-β-glucoside, in beans of *Phaseolus lunatus*; **lotusin** from *Lotus aribicus.*

Salicin, $C_{13}H_{18}O_7$, found in varieties of Salix, is hydrolysed to saligenin (*o*-hydroxy-benzyl alcohol) and dextrose; **populin** or *benzoyl-salicin*, $C_{10}H_{22}O_8$ (in varieties of Populus), can be prepared artificially from benzoyl chloride and salicin.

Arbutin, $C_{12}H_{16}O_7$, and **methyl-arbutin,** $C_{13}H_{18}O_7$, present in the leaves of the bear-berry, &c., yield glucose and quinol or methyl-quinol respectively. Methyl-arbutin has been synthesised by *Michael* (B. 1881, **14,** 2097) from acetochloroglucose and quinol methyl ether.

Hesperidin, $C_{22}H_{26}O_{12}$, which is contained in unripe oranges, &c., can be decomposed into glucose, hesperetic acid (isomeric with ferulic acid, p. 495), and phloroglucinol.

Phloridzin, $C_{21}H_{24}O_{10}$, found in the bark of fruit-trees, yields glucose and **phloretin,** $C_{15}H_{14}O_5$, and this latter, in its turn, phloretic acid and phloroglucinol (p. 449). For structure cf. J. C. S. 1930, 21. Both induce glycosuria (a functional derangement of the liver, producing temporary diabetes) in animals.

Aesculin, $C_{15}H_{16}O_9$, present in the bark of the horse-chestnut, is decomposed by acids into grape-sugar and Aesculetin (dihydroxy-coumarin), $C_9H_{16}O_4$.

Digitonin, digitalin, and **digitaleïn** are three glucosides which, together with **digitoxin** (the most important constituent from a pharmacological point of view), are present in the digitalis of commerce (cf. B. **24,** 339; **25,** Ref. 680; **31,** 2454).

Coniferin, $C_{16}H_{22}O_8 + 2H_2O$, contained in the cambium sap of the Coniferæ, yields glucose and coniferyl alcohol on hydrolysis, and serves for the preparation of vanillin (p. 459).

Indican (p. 560) is indoxyl-glucoside.

Syringin, the glucoside of Syringa, is a methoxy-coniferin.

Myronic acid, $C_{10}H_{17}O_9NS_2$, is present as potassium salt (*Sinigrin*), $C_{10}H_{16}KO_9NS_2$, H_2O (glistening needles), in black mustard seed. It is hydrolysed by baryta water, or by my-

rosin, an enzyme present in mustard seed, to *d*-glucose, potassium bisulphate, and allyl isothiocyanate (p. 286).

(For list of natural glucosides cf. *Armstrong*, "Simple Carbohydrates and Glucosides", p. 80.)

A complex glucoside is **Solanine S.**, $C_{54}H_{96}O_{18}N_2$, H_2O, from *Solanum sodomacum*, as on hydrolysis it yields Solanidine S., $C_{18}H_{31}ON$, *d*-glucose, *d*-galactose, and *d*-methyl-pentose.

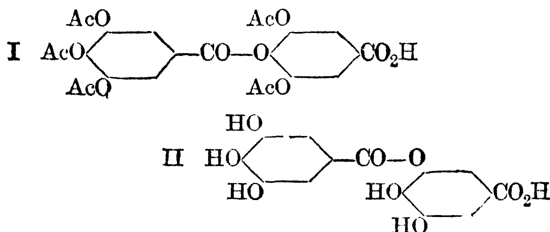
The colouring matters of many plants, viz. the red, blue, and violet pigments, soluble in alcohol and water but insoluble in ether, and known as **anthocyanins**, are of glucosidic structure (*Willstätter* and *Everest*, A. 1913, **401**, 189). The pigment of the cornflower contains one glucose and one cyanidin residue, that of the cranberry contains one cyanidin and two galactose residues. Delphinin, pelargonin, and myrtilin are all glucosides. (For the products of hydrolysis compare p. 580, and for general survey, *Stewart*, Rec. Adv. 1927, **2**, 172.)

Gallotannic acid, derived from nut galls and one of the best-known tannins (p. 490), is a glucoside, and yields *d*-glucose and gallic acid when hydrolysed with dilute mineral acids. The tannin of Chinese galls is a gallic acid derivative, and its structure, according to *Fischer*, is that of a penta-acylated glucose, the particular acyl group being the digalloyl group; it is therefore **pentadigalloyl glucose**, $C_6H_7O_6[CO{\cdot}C_6H_2(OH)_2{\cdot}O{\cdot}CO{\cdot}C_6H_2(OH)_3]_5$. Several products analogous in structure have been synthesised by *Fischer* and *Freudenberg* (B. 1912, **45**, 912, 2709), and have been shown to resemble natural tannin in many respects.

The first step in the synthesis consists in protecting the hydroxyl group of gallic acid, either by acetylation or by conversion into its triethylcarbonato derivative, $CO_2H{\cdot}C_6H_2(O{\cdot}CO_2Et)_3$, by the aid of ethyl chloroformate, $Cl{\cdot}CO_2Et$ (p. 289). The protected acid is next converted into the acid chloride, $COCl{\cdot}C_6H_2(OAc)_3$ or $COCl{\cdot}C_6H_2(O{\cdot}CO_2Et)_3$, which can be condensed with *d*-glucose in the presence of an organic base, and by subsequent elimination of the acetyl or carbethoxy groups, by careful hydrolysis pentagalloyl glucose is obtained. Galloyl derivatives of glycerol, erythrytol and mannitol have been prepared by similar methods, and all have the property of precipitating gelatine in much the same manner as tannin.

To introduce *p*-digalloyl groups into glucose the following series of reactions are carried out:—Gallic acid → triacetyl-

gallic acid → triacetylgalloyl chloride. The latter is then condensed in the presence of dilute alkali with 3:5-diacetylgallic acid, $CO_2H \cdot C_6H_2(OH)(OAc)_2$, a product obtained by the partial hydrolysis of the triacetylated acid. By this condensation penta-acetyl-digallic acid (I) is obtained. This acid is



converted into its acid chloride by means of PCl_5, and the pentacetyldigalloyl chloride then condensed with *d*-glucose, and the acetyl groups removed from the final condensation product by hydrolysis with methyl alcohol and concentrated hydrochloric acid, or by means of a little sodium ethoxide, and β-pentadigalloylglucose is thus obtained. This closely resembles the tannin from Chinese galls, but has a slightly different optical rotation. They were also able to show that by methylating gallic acid, preparing pentamethyl-*p*-digalloyl chloride. and condensing this with glucose, a product is formed which is identical with the methyl tannin obtained by the action of diazomethane on natural Chinese tannin (B. 1913, **46**, 1116).

During the course of the work it was proved that when penta-acetyl-*p*-digallic acid (I) is hydrolysed, the product is not the corresponding *p*-digallic acid, but the isomeric *m*-digallic acid (II) (B. 1913, **46**, 1116; 1918, **51**, 45).

A simple **glucogallic acid** can be isolated from Turkish gall nuts; it is a condensation product derived from one molecule of glucose and one of gallic acid, and can be methylated. The methyl derivative has no reducing properties, and when hydrolysed by methyl alcoholic potash yields gallic acid trimethyl ether, and hence the conclusion is drawn that this natural product is formed by the condensation of the glucose molecule with the carboxylic group of the gallic acid (*Feist* and *Haun*, Arch. Pharm., 1913, **251**, 468):



$$(OH)_3C_6H_2 \cdot CO \cdot O \cdot \overset{\lceil\quad O \quad\rceil}{CH[CH \cdot OH]_3 \cdot CH} \cdot CH_2 \cdot OH.$$

A synthetic product, β-glucisido-tannic acid, obtained by *Fischer* (B. 1912, **45**, 3773), is not identical, and probably has the ether constitution:



$$CO_2H \cdot C_6H_2(OH)_2 \cdot O \cdot \overset{\lceil\!\!\text{———}\, O \,\text{———}\!\!\rceil}{CH[CH \cdot OH]_3 \cdot CH} \cdot CH_2 \cdot OH.$$

The products formed from hydroxy aromatic acids by the condensation of the COOH group of one molecule with the phenol group of a second are termed by *Fischer* **depsides,** and di-, tri-, and tetra-depsides can be obtained according to the number of molecules of acid thus condensed together to form a chain. Such depsides are esters derived from phenols, and, as such, can be hydrolysed.

The **Saponins** are a group of glucosides widely distributed in the vegetable kingdom. They are soluble in water, insoluble in ether, form emulsions with oils, and prevent the deposition of finely-divided particles. They have a bitter acrid taste and are characterized by giving a soapy foam when shaken with water, and by their toxic action on cold-blooded animals. When hydrolysed they yield a sugar or sugars and **sapogenins,** which are complex carbon compounds of unknown structure. The soapwort (*Saponaria officinalis*) root contains saporubin $(C_{18}H_{28}O_{10})_4$, which on hydrolysis gives sugars and the sapogenin, $C_{14}H_{22}O_2$.

All the natural and synthetic glucosides can be divided into two groups, α and β, corresponding in structure with the two stereoisomeric methylglucosides, and they are readily distinguished by their behaviour towards certain enzymes. Thus all β-glucosides—and practically all the natural glucosides belong to this group—are readily hydrolysed by water in the presence of emulsin (p. 647), whereas the α-glucosides are hydrolysed by maltase, but not by emulsin. Within recent years numerous glucosides have been synthesised by means of enzymes. Compare Chap. XLVIII, B.

The common sugar present in natural glucosides is *d*-glucose, but *d*-galactose, rhamnose, and arabinose are also found. A convenient method for ascertaining the sugar present, when it is found difficult to isolate it, is to study the rates of hydrolysis of the glucoside in the presence of different sugars. Most of the sugars will have no influence on the rate of hydrolysis, but one particular sugar will produce a retardation of the hydrolysis, and this may be accepted as the one present in combination in the particular glucoside.

XLIII. ALBUMINS; PHYSIOLOGICAL CHEMISTRY

An extended description of the substances (other than those already mentioned) which are found in the animal organism, and which are therefore of importance for physiological chemistry, will not be attempted here, since they are for the most part better known from a physiological than from a chemical point of view. Only the albumins and some of the substances which are produced during metabolic processes will be dealt with.

Albumins

For an account of the chemistry of albumins see *A. Kossel* (B. 1901, **34**, 3214; *E. Fischer*, B. 1906, **39**, 530).

The albumins make up the chief part of the organism, being present partly in the soluble and partly in the solid state; they are found in protoplasm and in all the nutritive fluids of the body. In the tissues of green plants the albumins are synthesised in quite unknown ways from simple substances like carbon dioxide, water, ammonium nitrate and sulphate. (Cf. *Meldola*, J. C. S. 1906, 749.) The majority of albumins are insoluble in water, but dissolve in dilute saline solutions. Their presence in the juices of the animal organism is probably due to saline and other substances. In solution they are opalescent, lævo-rotatory, and do not diffuse through parchment paper, *i.e.* are colloids; but they are thrown down when the solution is warmed, or upon the addition of strong mineral acids, of many metallic salts [*e.g.* copper sulphate, basic lead acetate, and mercuric chloride], of alcohol, tannic acid, acetic acid together with a little potassium ferrocyanide, picric acid, or phosphotungstic acid. They are insoluble in alcohol or ether, and their solutions are usually precipitated ("salted out") by the addition of ammonium sulphate, and mixtures of different albumins can often be fractionally precipitated by gradually increasing the concentration of the ammonium sulphate. This concentration is definite for each albumin, as is also its temperature of coagulation. Proteins can also be coagulated by treatment with absolute alcohol or with boiling water. After coagulation all albumins become insoluble in neutral solvents, but dissolve in alkalis or acids, yielding **metaproteins,** which are also formed by boiling the

uncoagulated albumins with acetic acid or alkali. When boiled: (*a*) with nitric acid, they are coloured yellow (the xantho-proteïn reaction): (*b*) with a solution of mercuric nitrate containing nitrous acid (*Millon's reagent*), red; (*c*) with caustic soda solution and a very little cupric sulphate, violet.

Many of the albumins have been prepared pure, although this is a very difficult operation. With the exception of the crystalline albumin which occurs in hemp, castor-oil, and pumpkin seeds (B. **15,** 953), and the recently isolated crystalline egg albumin and serum albumin (B. **24,** Ref. 469; **25,** Ref. 173), and ovalbumin, they do not crystallize.

The different albumins vary only slightly among themselves in percentage composition; they contain:

C = 52·7 to 54·5 p.c.; H = 6·9 to 7·3 p.c.; N = 15·4 to 17·6 p. c.; O = 20·9 to 23·5 p.c.; and S = 0·8 to 5·0 p.c.

It is impossible at present to construct a formula from these numbers, and even approximate molecular weights have not been determined.

The fact that albumin contains sulphur is worthy of note, though the mode in which it is combined in the molecule is unknown; warming with a dilute alkaline solution is sufficient to eliminate it partially, *e.g.* when white of egg is boiled with an alkaline solution of lead oxide, sulphide of lead is precipitated (the test for sulphur in albumin).

Albumin preparations usually leave a very considerable amount of ash, *i.e.* inorganic salts, on incineration. It is not yet certain in how far this mineral matter forms an integral constituent of these substances; but the properties of "egg albumin free from ash" are materially different from those of ordinary albumin (B. **25,** 204).

Although the constitution of no single albumin has been determined, a considerable amount of work has been done in this direction, more especially by an examination of the simpler products obtained when the albumins are (*a*) oxidized, (*b*) hydrolysed, and (*c*) fermented by micro-organisms.

(*a*) The products obtained on oxidation consist largely of volatile fatty acids, their aldehydes, ketones, and nitriles, together with hydrogen cyanide and benzoic acid.

(*b*) The usual hydrolytic agents used are (1) baryta water, (2) hydriodic acid, (3) concentrated hydrochloric acid, and (4) sulphuric acid (25 per cent). The last of these appears to

be the best, as it produces less complex decomposition, *e.g.* less ammonia and more amino-acids. The most marked feature of the products thus obtained is the predominance of amino-acids.

The list of compounds which have been isolated from the hydrolytic products is as follows: (i) Ammonia; (ii) carbamide; (iii) diamino-acids; (iv) monamino-acids; (v) pyrrolidine-2-carboxylic acid (proline), $HN\left\langle\begin{array}{l}CH_2\text{———}CH_2\\ CH(CO_2H)\cdot CH_2\end{array}\right.$, and its hydroxy derivative (oxyproline); (vi) furaldehyde (p. 550); (vii) histidine (iminazole-alanine), $C_6H_9O_2N_3$; (viii) arginine, or δ-guanino-α-amino valeric acid, $NH_2\cdot C(:NH)\cdot NH\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH(NH_2)\cdot CO_2H$, which has been synthesised from ornithine (p. 497) and cyanamide (p. 286); (ix) tryptophan (indol-alanine); (x) tyrosine (p. 489); (xi) purin derivatives, *e.g.* guanine or 2-amino-6-oxypurine and adenine or 6-amino-purine; (xii) Pyrimidine derivatives, *e.g.* cytosine or 3-amino-1-pyrimidone and thymine or 4-methyl-3-keto-2:3-dihydro-1-pyrimidone.

Of the diamino-acids the following are the more important: Diamino-acetic acid from caseïn, αδ-diamino-valeric acid or ornithine, αε-diamino-*n*-caproic acid or lysine.

Of the monamino-acids: Glycocoll, and derivatives such as skatolglycocoll, α-amino-propionic acid or alanine, α-amino-isobutylacetic acid or leucine, α-amino-isovaleric acid or valine, α-amino-succinic or aspartic acid, α-amino-glutaric or glutamic acid, phenylalanine or β-phenyl-α-amino-propionic acid, $CH_2Ph\cdot CH(NH_2)\cdot CO_2H$, α-amino-α-hydroxy-propionic acid or serine, α-amino-α-thiolactic acid or cysteïn, and the corresponding disulphide or cystin, β-hydroxy-phenyl-α-amino-propionic acid, and β-hydroxy-glutamic acid.

Certain albumins also yield carbohydrates, more especially amino-sugars, *e.g.* glucosamine, $C_6H_{11}O_5\cdot NH_2$ from chitin.

A method of separating the hydrolytic products is to esterify and fractionally distil under reduced pressure.

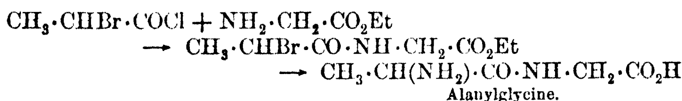
A few simple proteins yield only a single amino-derivative; thus both **salmine** and **clupeine,** obtained respectively from the testicles of the salmon and herring, yield histidine. As a rule, the more complex proteins yield a considerable number of amino-compounds, the number of such compounds and also their relative proportions varying with the protein.

The amount of hydrolytic products actually isolated and belonging to the twelve groups given above is frequently more than 90 per cent of the protein employed (*e.g.* gelatin and zein) and consists mainly of open chain compounds.

The carboxylic groups present in the hydrolytic products are probably not present in the original molecule, and it is highly probable that most of the amino-groups are not present as such, but are employed in uniting the various radicals together, since only some 10 per cent of the total nitrogen in albumin is eliminated as such on treatment with nitrous acid; in other words, the amino-group of one molecule reacts with the carboxylic group of another, yielding compounds with the group, ·CO·NH·, characteristic of acid amides. *Emil Fischer* and others have synthesised complex compounds of this type by the gradual condensation of amino-acids. Although none of the proteins has been so far synthesised, the products—the **polypeptides**—exhibit considerable analogy to the peptones.

The following general methods are used for the synthesis of polypeptides:—

1. The chloride of a halogenated fatty acid is condensed with the ester of an amino-acid, the resulting ester hydrolysed, and the halogen then replaced by an amino-group by means of ammonia:



$$CH_3{\cdot}CHBr{\cdot}COCl + NH_2{\cdot}CH_2{\cdot}CO_2Et \rightarrow CH_3{\cdot}CHBr{\cdot}CO{\cdot}NH{\cdot}CH_2{\cdot}CO_2Et \rightarrow CH_3{\cdot}CH(NH_2){\cdot}CO{\cdot}NH{\cdot}CH_2{\cdot}CO_2H$$

Alanylglycine.

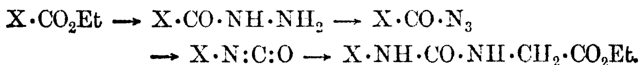
2. The dipeptide thus obtained can be converted into its acid chloride, and this condensed with a molecule of an ester of an amino-acid, *e.g.* glycine ester, yielding the compound $CH_3{\cdot}CH(NH_2){\cdot}CO{\cdot}NH{\cdot}CH_2{\cdot}CO{\cdot}NH{\cdot}CH_2{\cdot}CO_2C_2H_5$, which on careful hydrolysis yields the corresponding acid—**alanylglycylglycine**—an example of a tripeptide. The operations can be repeated, and in this way compounds containing 18 amino-acid residues have been synthesised.

As the amino-acids obtained by hydrolysing natural proteins are optically active, *Fischer* used optically active acids and esters in his synthetical operations, the optically active acid being obtained by resolving its racemic benzoyl derivative by means of active bases and then removing the benzoyl group.

3. A modification of the above synthesis consists in converting an amino-acid into its acid chloride by means of acetyl chloride and phosphorus pentachloride, and then condensing this chloride with a molecule of an amino-acid.

4. Glycylglycine can be obtained by heating ethylglycine when the anhydride, diketopiperazine, $NH<\begin{matrix}CO\cdot CH_2\\CH_2\cdot CO\end{matrix}>NH$, is formed, and hydrolysing this with dilute alkali.

5. Another method of obtaining polypeptides is through the azide (p. 192) of the acid. Thus starting with ethyl hippurate, this is converted into the hydrazide, and, finally, into the azide, which yields a carbimide when heated. The carbimide is condensed with the ester of an amino acid, *e.g.* ethylglycine, yielding a product which can be transformed into an azide and the series of reactions repeated (*Curtius*, J. pr., 1916, **94**, 85).



$$X\cdot CO_2Et \rightarrow X\cdot CO\cdot NH\cdot NH_2 \rightarrow X\cdot CO\cdot N_3 \rightarrow X\cdot N{:}C{:}O \rightarrow X\cdot NH\cdot CO\cdot NH\cdot CH_2\cdot CO_2Et.$$

Fischer succeeded in synthesising by his methods a polypeptide containing 18 amino-acid group, viz. *l*-leucyl-triglycyl-*l*-leucycl-triglycyl-*l*-leucyl-octaglycyl-glycine with a molecular weight of 1213.

The position of the free amino-group in a complex polypeptide can be ascertained by the action of naphthalene-β-sulphonyl-chloride, and hydrolysis with hydrochloric acid. Thus, alanyl-glycylglycine (a tripeptide) treated in this way gives naphthalene-β-sulphonylalanine and glycine as hydrolytic products, indicating that the free amino-group is present in the alanyl residue (B. 1916, **49**, 2449, 2838).

The optical rotation of an active polypeptide kept in contact with dilute alkali for a few days changes and this has been shown to be due to the enolisation of an inner—CHR·CO—group. In the case of a tripeptide the products of hydrolysis, viz. the inactive amino-acid isolated, will prove that this occupied the middle of the peptide chain.

A few polypeptides, *e.g.* tetrapeptides, have been isolated from the hydrolytic products of certain proteins.

(*c*) The putrefaction of albumins gives rise not only to amino-acids, but also to aromatic and fatty acids (*e.g.* butyric acid, phenyl-acetic acid), indole, skatole, and cresol; further, to the basic **ptomaïnes** (the toxines produced in dead bodies), which

include putrescine (from arginine) and cadaverine (from lysine), choline, muscarine, and neurine (p. 202). All of these are not poisonous, and many also occur in the vegetable kingdom. Only the amines derived from phenylalanine tyrosine, tryptophan and histidine have marked physiological activity, and histamine derived from histidine is the most active. For a compilation of the ptomaïnes, see *Brieger*, Archiv. f. patholog. Anatomie, **115**, 483.

The enzyme pepsin present in stomach juices converts albumins at 30–40° into **anti-** and **hemi-albumoses**, both of which then pass into peptone; trypsin, an enzyme of the pancreas, also gives the two above albumoses, but then transforms the anti-compound into peptone and the hemi-compound into leucine, tyrosine, aspartic acid and glutamic acid (the pancreatic digestion; for details, see *Kühne*, B. **17**, Ref. 79). The peptones are readily soluble in water, diffuse quickly through vegetable parchment, and they are neither coagulated upon heating nor by most of the reagents which coagulate albumin, *e.g.* ammonium sulphate, whereas the albumoses are precipitated by this reagent. These reactions indicate that the albumoses are intermediate between the albumins proper and the simple decomposition products already mentioned, and that the peptones are intermediate between the same decomposition products and the albumoses. Both albumoses and peptone possess acidic and basic properties, and may be esterified by means of alcohol and hydric chloride, hence they probably contain carboxylic groups.

The different albumoses, *e.g.* hetero- and proto-albumoses, must differ considerably as regards constitution, as the former yields glycocoll, much arginine, but little histidine, and very little tyrosine and indole on hydrolysis, whereas the latter yields no glycocoll, equal amount of arginine and histidine, and much tyrosine and indole.

Other methods adopted are to introduce chemical substances into the animal system intravenously or *per os*, and then to examine in what form the compound is excreted from the system; as examples, bromobenzene is excreted as bromophenyl-mercapturic acid, and various terpene derivatives are excreted in combination with glycuronic acid.

When soluble salts of iron are allowed to act upon white of egg and upon peptone, **iron albuminate** and **iron peptonate** are respectively produced, these being employed in medicine

as iron preparations for internal use under the names of *liquor ferri albuminati* and *peptonati*.

The following scheme of nomenclature for proteins is accepted by most English-speaking chemical and physiological societies:—

1. **Protamines.**—The simplest proteins, they include **salmine, sturine,** &c., isolated from fish testicles.

2. **Histones.**—These are somewhat more complex than the protamines. They can be precipitated by ammonia.

3. **Albumins,** *e.g.* egg albumin, serum albumin from blood and nutritive fluids, and lact-albumin from milk. These are crystalline, dissolve in water, and are not precipitated by common salt. They coagulate at 70°-75°.

4. **Globulins** are insoluble in water but dissolve in dilute salt solution. They can be salted out by means of magnesium sulphate. Examples: **Globulin** from the crystalline lens of the eye, **fibrinogen** from blood; **fibrin** from clotted blood, and **myosin** from the plasma of living muscle are globulin derivatives. They are extremely common in higher plants, *e.g.* **legumin** from seeds of various *Leguminosæ*, **edestin** of *Cannabis sativa*, **conglutin** from seed of lupins.

5. **Gluteins** are proteins of vegetable origin. They are soluble in alkalis, and are closely allied to the globulins.

6. **Gliadins.**—Vegetable proteins, soluble in alcohol, *e.g.* glutein from wheat and hordein from barley.

7. **Phospho-proteins**, *e.g.* caseinogen, the principal protein of milk; casein obtained from caseinogen by the action of rennet. They are acidic and do not coagulate.

8. **Sclero-proteins.**—Mainly insoluble proteins, which form the skeletal parts of tissues, *e.g.* gelatin from cartilages, chondrin, elastin from ligaments, and keratin from hoofs, nails, hair, &c. Sponge and coral contain similar substances.

9. **Conjugated proteins** consist of compounds containing a protein molecule united to some other group.

(*a*) **Nucleo-proteins** are important constituents of the cell nucleus, *e.g.* of pus cells, blood corpuscles, and yeast cells. They are insoluble in water or acids, but dissolve in alkalis, and contain combined phosphoric acid. On hydrolysis they yield a protein and nucleïn, and the latter on further hydrolysis yields a second protein and nucleïc acid, and this last yields the nucleïn bases, viz. adenine, hypoxanthine, guanine, and xanthine (p. 302).

Nucleïc acid may also be transformed into nucleïn bases by various enzymes present in the different organs of the animal system. Recent work renders it highly probable that at least three distinct enzymes take part in such transformations: (*a*) an oxidase; (*b*) adenase, which transforms adenine into hypoxanthine and xanthine; (*c*) guanase, which transforms guanine into xanthine.

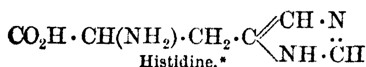
(*b*) **Chromo-proteins** or **Hæmoglobins.**—**Hæmoglobin** is the colouring matter of the red blood corpuscles. It can be decomposed into globin and hæmatin (see below). Hæmoglobin combines very readily with oxygen, *e.g.* in the lungs, to **oxy-hæmoglobin,** which yields up its oxygen again, not only in the organism, but also in a vacuum and when exposed to the action of reducing agents, *e.g.* ammonium sulphide. With carbon monoxide it combines to the compound, **carbon-monoxide-hæmoglobin.** All three compounds can be obtained crystallized in the cold, and they possess characteristic absorption spectra. **Hæmin,** $C_{33}H_{32}O_4N_4FeCl$, is obtained in the form of characteristic microscopic, reddish-brown crystals by the action of glacial acetic acid and some common salt upon oxy-hæmoglobin; this is a delicate test for the presence of blood. **Hæmatin,** a dark-brown powder containing 8 per cent of iron, is obtained by the spontaneous decomposition of hæmoglobin, or by the action of alkalis on hæmin, and contains OH in place of the Cl atom of hæmin. **Hæmatoporphyrin,** $C_{33}H_{38}O_6N_4$, is the product formed by the action of hydrobromic acid on hæmin.

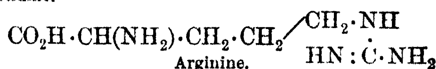
(*c*) **Gluco-proteins.**—The **mucins** yield albumin and carbohydrate on hydrolysis; they are insoluble in water, but possess acidic properties. The percentage of nitrogen is less than in the ordinary albumins.

10. **Protein derivatives,** or the products of protein hydrolysis. (*a*) **Meta-proteins.**—This includes the substances previously known as alkali-albumins and acid-albumins. (*b*) **Proteoses,** including albumoses, globuloses, and gelatoses. (*c*) **Peptones** (cf. p. 657). (*d*) **Polypeptides** (cf. p. 655). Both *b* and *c* may be mixtures of polypeptides.

The changes which protein foodstuffs undergo in the animal system have been the subject of much study (*Hopkins*, J. C. S. 1916, **109,** 629). It is generally agreed that the proteins are hydrolysed in the intestine to their ultimate constituents, the amino or imino acids, and that these acids are absorbed by

the blood and carried to the different tissues, where they can undergo (1) synthesis to protein compounds, (2) oxidation if present in abundance, and (3) conversion to purin derivatives, adenine and guanine, and the excretory substances, allantoin and uric acid. This conclusion is largely based on the following facts:—(*a*) completely hydrolysed proteins, *e.g* casein, are as effective as nutrients as the unhydrolysed proteins; (*b*) in the blood the bulk of the organic nitrogen is present as amino acids and not as complex polypeptides or proteins (this has been proved by van Slyke by measurements of nitrogen evolved by the action of nitrous acid on the blood); (*c*) when food proteins are introduced intact into the blood, reactions follow which are quite different from those which follow the normal ingestion of food. Experiments made on rats to determine which particular amino acids are essential indicate that with tryptophan absent, but all the other hydrolytic products present in the food, growth ceases and death finally ensues. Similarly arginine or histidine must be present, but not necessarily both. On the other hand, the removal of glutamic and aspartic acids from the hydrolysed food does not prevent growth. It is thus clear that the animal system is incapable of synthesising the indole group (tryptophan), or the guanidine (arginine), or iminazole (histidine) groups, and it is essential that the food supplied should contain such groups. If arginine is supplied, the system appears to be capable of converting this into histidine; the close relationship between the two compounds is illustrated in the two formulæ:—





Cf. also J. Bio. C. 1924, **59**, 577; 1924, **61**, 747.

*For synthesis see *Pyman*, J. C. S. 1916, **109**, 186; and for synthesis of **Carnosine** β-alanylhistidine,



cf. also *Barger* and *Tutin*, Bio. J. 1918, **12**, 402; it occurs in Liebig's extract of beef.

The fatty material of foods undergoes degradation in the body, probably first hydrolysis by the enzyme lipase and then progressive oxidation. It was thought at one time that this oxidation occurred solely at the β-carbon atom and thus shortening the acid chain by two carbon atoms. Oxidation at γ and δ carbon atom can also occur in vitris and also possibly in the body (*Clutterbuck* and *Raper*, Bio. J. 1925, 384; *Hurtley*, J. Bio. C. 1908, 77, 221, 227, 419). The intermediate products are probably keto-acids.

Asparagin plays an important part in plant metabolism, all reserve ammonia in tissues is probably transformed into this, and it is probably the form in which nitrogen is translocated in the plant.

Glutathione, a dipeptide of cystine and glutamic acid, probably $SH \cdot CH_2 \cdot CH(CO_2H) \cdot NH \cdot CO \cdot CH_2 \cdot CH_2 \cdot CH(NH_2) \cdot CO_2H$, is an important factor in oxidative changes in muscle tissue. If the dipeptide is removed by washing no absorption of oxygen by the tissue, and no elimination of carbon dioxide occurs unless the glutathione removed is restored (*Hopkins* and *Dixon*, J. Bio. C. 1922, **54,** 527.)

Another sulphur amino acid, **methionine,** $CH_3S \cdot CH_2 \cdot CH_2 \cdot CH(NH_2) \cdot CO_2H$ has been synthesised by *Barger* and *Coyne*.

Vitamins.—For animal nutrition small amounts of compounds known as vitamins or advitants (*Armstrong*) are essential in the diet. The amounts required are extremely small. There appear to be at least five separate compounds, A, B, C, D, E. Two of these, B and C, are soluble in water, and the remaining three in oils. Very little is known of their chemical nature.

Vitamin A is formed primarily in green plants, and is usually associated with natural fats or oils, and is soluble in the usual fat solvents. It cannot be saponified, and is present in the non-saponifiable fractions of fats and oils, more particularly in fish-liver oils and in milk. Crude **carotene,** $C_{40}H_{56}$, a plant pigment, is highly active as a vitamin, but its activity diminishes as the pigment is purified. The absence of this vitamin in the diet induces lack of growth in the animal system.

Vitamin B has been shown to be a mixture of at least three distinct substances, B1, B2 and B3. B1, present in rice polishings, wheat germ and yeast, so far as is known appears to be a fairly simple nitrogenous base. Its absence in a diet retards growth, produces beri-beri in the human system, and so-called

polyneuritis in pigeons. B2, from lean liver meat and brewer's yeast, and B3, from certain yeast extracts, are also important factors in animal growth, but little is known of their chemical nature.

Vitamin C, present in the juices of limes, lemons, oranges, &c., can be obtained in a concentrated form by fractional precipitation. Its absence in diet tends to produce scurvy and nothing is known of its chemical nature.

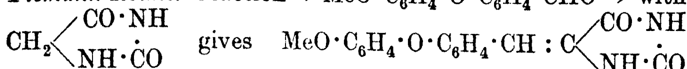
Vitamin D, the bone-forming vitamin. Its absence in the diet of young animals produces rickets. It is present more especially in cod liver oil and in materials rich in sterols after irradiation by ultra-violet light. Actual exposure of the body tissue to ultra-violet rays has much the same effect as administration of vitamin D in the diet. The vitamin appears to be formed by the action of ultra-violet rays on **ergosterol**, a sterol accompanying cholesterol, the common sterol present in the non-saponifiable fraction from animal fats and oils. *Heilbron* and *Sexton* (J. C. S. 1929, 921) have suggested a possible structural formula for ergesterol and it appears probable, from a study of absorption spectra, that the conversion of this into Vitamin D is not of a very complex type. Irradiated ergosterol is now a commercial product used, for example, as a substitute for cod liver oil, and for admixture with margarine, which, normally derived from vegetable oils, contains little or no Vitamin D.

Vitamin E, necessary for the development of the reproductive system, is present in the non-saponifiable fraction of wheat germ oil, and is not removed when the phytosterol (the common plant sterol) is eliminated. It is fairly stable, and nothing is known of its chemical nature.

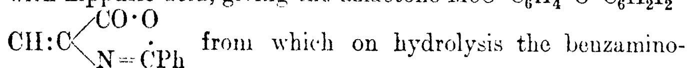
For general survey of Vitamins, see *Drummond*, J. Ind. 1930, 1T.

Hormones.—The internal glands in the animal system give rise to secretions and from some of these definite chemical entities, with characteristic physiological properties, have been isolated, and in some cases synthesised in the laboratory; among these may be mentioned (1) *l*-**Adrenaline** from the suprarenal glands (cf. Chap. LIV, C). (2) **Thyroxin,** $C_{15}H_{11}O_4NI_4$, from the thyroid gland (0·02 per cent yield). Its structure as the 3:5:3′:5′-tetraiodo derivative of *p*-hydroxyphenyl ether of tyrosine (II) has been established as the result of the following synthesis (cf. *Harrington*, Bio. J. 1926, 300; J. Ind.

1926, 931) $MeO\cdot C_6H_4Br + HO\cdot C_6H_5 \rightarrow MeO\cdot C_6H_4\cdot O\cdot C_6H_5$. *Tiemann-Reimer* reaction $\rightarrow MeO\cdot C_6H_4\cdot O\cdot C_6H_4\cdot CHO \rightarrow$ with



and this on hydrolysis gives (II) the *p*-hydroxy-phenyl ether of tyrosine $HO\cdot C_6H_4\cdot O\cdot C_6H_4\cdot CH_2\cdot CH(NH_2)\cdot CO_2H$ (II) which with iodine yields thyroxin. Another synthesis consists in condensing quinol monomethyl ether with 3:4:5-triodonitrobenzene to 2:6-diiodo-4-nitro-4′-methoxy-diphenyl ether $MeO\cdot C_6H_4\cdot O\cdot C_6H_2I_2NO_2$. This can be transformed into the amine, then the nitrile and finally into the aldehyde, $MeO\cdot C_6H_4\cdot O\cdot C_6H_2I_2\cdot CHO$, which condenses with hippuric acid, giving the azlactone $MeO\cdot C_6H_4\cdot O\cdot C_6H_2I_2\cdot$



cinnamic acid $MeO\cdot C_6H_4\cdot O\cdot C_6H_2I_2\cdot CH:C(NHCOPh)CO_2H$ is formed. This with hydriodic acid and phosphorus yields $HO\cdot C_6H_4\cdot O\cdot C_6H_2I_2\cdot CH_2\cdot CH(NH_2)\cdot CO_2H$ from which thyroxine can be obtained by treatment with iodine in ammoniacal solution. The *dl*-compound has been resolved by means of *l*-α-phenylethylamine. (3) **Insulin** from the internal secretion of the pancreas is used for injection in cases of diabetes. It appears to produce an accelerated combustion of sugar in the system and the synthesis of a further supply of glycogen and of glucosone. The hormone has been isolated in a crystalline form and the simplest formula suggested is $C_{45}H_{69}O_{14}N_{11}S, 3H_2O$, and it is probably a complex protein derivative.

For theories of the natural syntheses of vital products see Chap. IX. Vol. II, "Recent Advances in Organic Chemistry" by Stewart, 1927.

Chlorophyll, the colouring matter of green plants, is closely related to hæmatin, and much work has been done to ascertain its structure, particularly by *Willstätter* and his pupils (for summary cf. B. 1914, **47**, 2831). It consists of two substances, α = $COOCH_3\cdot(C_{32}H_{30}ON_4Mg)COOC_{20}H_{39}$, $^1/_2H_2O$, and β = $COOCH_3(C_{32}H_{28}O_2N_4Mg)COOC_{20}H_{39}$, and when either is hydrolysed with alkali, methyl alcohol, phytyl alcohol, and the salt of a tribasic acid chlorophyllin are formed. If alcohol is used for extracting chlorophyll from green leaves the crystalline product contains an ethyl in place of the phytyl group

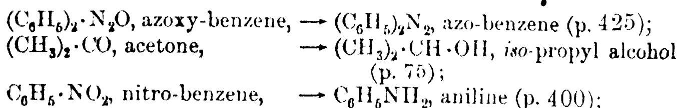
owing to alcoholysis occurring under the influence of an enzyme chlorophyllase. The magnesium is removed from chlorophyll and its derivatives by treatment with acids, but not with alkalis, and the nature of the final degradation products points to the presence of four pyrrol nuclei.

For general survey see *Stewart*, Rec. Adv. 1927, **2**, 189.

Just as chlorophyll is the common colouring matter of green plant tissues, **hæmoglobin** is the common colouring matter of animal blood. When decomposed it yields an albumin (globin) and **hæmatin** or **hæm.** This contains iron in place of magnesium and this can be removed by treatment with acids; and the fact that when analogous degradation methods are employed, both hæmatin and chlorophyll yield the same actioporphyrin, $C_{31}H_{34}N_4$, indicates a certain similarity of structure. Cf. *Willstätter* and *M. Fischer*, Z. Physiol. 1913, **87**, 423; *Küster*, ibid. **88**, 377. For synthesis of hæmoglobin cf. *Hill* and *Holden*, Bio. J. 1926, 1326). Actioporphyrin has been synthesised from 2:3 dimethylethylpyrrole (A. 1926, **448**, 178).

XLIV. REDUCTION

Reduction is the name usually given to a reaction in which oxygen is withdrawn from or hydrogen added to a compound; in certain cases both of these processes occur. Numerous cases of reduction have been mentioned in the preceding chapters, as examples:



$(C_6H_5)_2 \cdot N_2O$, azoxy-benzene, $\rightarrow (C_6H_5)_2N_2$, azo-benzene (p. 425);
$(CH_3)_2 \cdot CO$, acetone, $\rightarrow (CH_3)_2 \cdot CH \cdot OH$, *iso*-propyl alcohol (p. 75);
$C_6H_5 \cdot NO_2$, nitro-benzene, $\rightarrow C_6H_5NH_2$, aniline (p. 400);

As the reaction is so general, a more detailed discussion of it is given in this chapter.

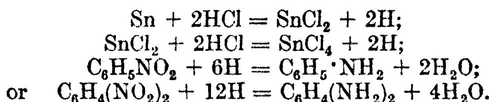
In addition to the above reactions, viz. withdrawal of oxygen or addition of hydrogen, the process previously referred to as inverse substitution (p. 33)—the replacement of halogen by hydrogen, *e.g.* $C_2H_5I \rightarrow C_2H_6$—is usually regarded as a type of reduction.

A. **Nascent Hydrogen.**—Of the numerous methods that can be employed for reduction, one of the commonest is by means of nascent hydrogen, *i.e.* hydrogen generated in the presence of the substance to be reduced. The fact that the majority of these reductions cannot be effected by means of ordinary gaseous hydrogen, but can be readily attained by the use of hydrogen at its moment of formation, is used as an argument in favour of the view that nascent hydrogen consists of the free atoms. As nascent hydrogen can be produced in a variety of ways, it follows that reductions by this method can be conducted under very varying conditions; and it is of extreme importance to note that the conditions are a prime factor in determining the nature of the product. It has already been pointed out that the reduction of nitro-benzene can give rise to azoxy-benzene, azo-benzene, phenyl-hydroxylamine, or aniline, according to the conditions under which the reaction occurs; and similar phenomena have been mentioned in the case of the reduction of terephthalic acid (p. 499).

Reductions by means of nascent hydrogen may take place in acid, alkaline, or neutral solution, and this affords a simple method of classification for these reactions.

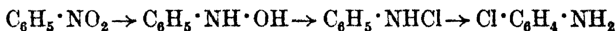
(*a*) **Reduction in Acid Solution.**—Almost any combination of acid and metal which gives rise to nascent hydrogen may be employed for this purpose; but the usual combinations are tin and hydrochloric acid, zinc and hydrochloric acid, zinc and acetic acid, zinc dust and acetic acid, iron and acetic acid.

The usual method employed in the laboratory for the reduction of nitro-compounds to the corresponding amino-compounds (see Aniline) is by means of tin and hydrochloric acid. The metal is first converted into stannous, and then into stannic chloride:



$$Sn + 2HCl = SnCl_2 + 2H;$$
$$SnCl_2 + 2HCl = SnCl_4 + 2H;$$
$$C_6H_5NO_2 + 6H = C_6H_5{\cdot}NH_2 + 2H_2O;$$
$$\text{or} \quad C_6H_4(NO_2)_2 + 12H = C_6H_4(NH_2)_2 + 4H_2O.$$

The method has certain objectionable features which render it unsuitable for use on the manufacturing scale. Among these may be mentioned (*a*) need for large excess of concentrated acid, and the fact that this acid will subsequently have to be neutralized. (*b*) The strong acid is liable to react with the reduction product, yielding halogenated amines. The introduction of the halogen into the benzene nucleus probably occurs in the following manner:—



$$C_6H_5{\cdot}NO_2 \rightarrow C_6H_5{\cdot}NH{\cdot}OH \rightarrow C_6H_5{\cdot}NHCl \rightarrow Cl{\cdot}C_6H_4{\cdot}NH_2$$

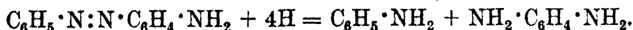
(*Bamberger*). Such chlorinated amines are always liable to be formed when concentrated hydrochloric acid is used in combination with a metal for the reduction of nitro-compounds. (*c*) The reduced compound often combines with the stannic chloride to form a double salt, *e.g.* $C_6H_5{\cdot}NH_2$, HCl, $SnCl_4$, and certain of these are somewhat difficult to decompose.

Aliphatic nitro-derivatives may also be reduced to amines by this method, except in cases where two nitro-groups are attached to the same carbon atom, when a ketone is formed. Other examples are the conversion of cyclic derivatives into hydro-derivatives, *e.g.* *p*-hydroxy-quinoline to tetrahydro-*p*-hydroxy-quinoline, and of sulphonic chlorides, $R{\cdot}SO_2{\cdot}Cl$, into thio-phenols, $R{\cdot}SH$.

In many cases tin-foil is stated to be preferable to granulated tin, as it exposes a larger surface, and occasionally alcoholic solutions of the hydrogen chloride are used in place of aqueous. Stannous chloride and hydrochloric acid occa-

sionally give better yields than tin and acid; thus nitromethane is reduced to methyl-hydroxylamine, and the method has been recommended for the estimation of nitro-groups. An excess of standard stannous chloride solution is used, and the excess titrated after the reduction is complete, each nitro-group requiring 3 gram molecules of stannous chloride.

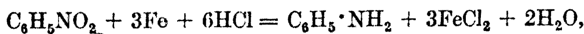
Stannous chloride is sometimes used without the addition of free acid; thus *Witt*, by reducing amino-azo-benzene with alcoholic stannous chloride, obtained aniline and *p*-phenylene-diamine:



$$C_6H_5\cdot N:N\cdot C_6H_4\cdot NH_2 + 4H = C_6H_5\cdot NH_2 + NH_2\cdot C_6H_4\cdot NH_2.$$

(Compare also *Jacobson*, A. 1895, **287**, 100.)

Most of the objections referred to in connection with the reduction of nitro-derivatives by means of tin and hydrochloric acid may be avoided by using iron and acetic acid or dilute hydrochloric acid. This method is usually adopted on the manufacturing scale, as only a small amount of acid, some one-fortieth of that indicated by the equation,



$$C_6H_5NO_2 + 3Fe + 6HCl = C_6H_5\cdot NH_2 + 3FeCl_2 + 2H_2O,$$

is required. The reason for this may be that the ferrous chloride reacts with the aniline and water, yielding ferrous hydroxide and aniline hydrochloride:



$$FeCl_2 + 2C_6H_5NH_2 + 2H_2O = Fe(OH)_2 + 2C_6H_5NH_2, HCl.$$

The hydrochloride then reacts with more iron, producing ferrous chloride and nascent hydrogen, which can reduce more of the nitro-compound (cf. p. 400).

The iron method possesses further advantages, as the reduction can be regulated much more readily than in the case of tin and acid. Thus *p*-nitro-acetanilide reduced by the iron method gives the corresponding amino-compound, $NH_2\cdot C_6H_4\cdot NH\cdot CO\cdot CH_3$, whereas with tin and hydrochloric acid hydrolysis and reduction both occur, and the product is *p*-phenylene-diamine.

Iron and acid may also be employed for the reduction of aromatic polynitro-compounds to amino-nitro-derivatives:



$$C_6H_4(NO_2)_2 \rightarrow NH_2\cdot C_6H_4\cdot NO_2,$$

but such a reduction is almost impossible with tin and acid.

Zinc, as granulated zinc, or more frequently as zinc dust, is

also used in conjunction with acids, usually hydrochloric or acetic. When concentrated hydrochloric is employed, chlorine is apt to enter the benzene ring (cf. p. 666); with glacial acetic acid (*Kraffts*, B. 1883, **16**, 1715) acetyl derivatives are formed occasionally instead of the simple reduction products. For example, when aldehydes are reduced, alkyl acetates and not alcohols are formed:



$$R{\cdot}CHO + 2H + CH_3{\cdot}CO_2H = R{\cdot}CH_2{\cdot}O{\cdot}CO{\cdot}CH_3 + H_2O,$$

and when nitro-derivatives are reduced, acetylated amines are obtained. Although aliphatic ketones cannot be reduced by this method, all ketones containing one or two benzene nuclei directly attached to the carbonyl group are readily reduced to pinacones (p. 199). Hydroxy-derivatives of anthraquinone may also be reduced in a similar manner, one or more of the hydroxy-groups being replaced by hydrogen, and aliphatic nitro-derivatives, such as nitro-guanidine, $NH{:}C(NH_2){\cdot}NH{\cdot}NO_2$, may be reduced to the corresponding amino-compounds.

Hydrochloric acid and amalgamated zinc reduce ketones of the type of acetophenone to the corresponding hydrocarbons, and the reaction is of special interest for the preparation of certain substituted phenols, *e.g.* *p*-ethylphenol, $OH{\cdot}C_6H_4{\cdot}CH_2{\cdot}CH_3$, from *p*-hydroxyacetophenone (B. 1913, 1837; 1914, 51).

A transformation occasionally effected by means of zinc dust and glacial acetic acid is the removal of two atoms of halogen and the conversion of a saturated compound into an olefine, *e.g.* tetramethyl-ethylene dibromide into tetramethyl-ethylene.



$$CMe_2Br{\cdot}CMe_2Br + 2H = 2HBr + CMe_2{:}CMe_2.$$

All peroxides (p. 188) are readily reduced by this method, *e.g.* diethyl-peroxide, Et_2O_2, to ethyl alcohol (or ethyl acetate).

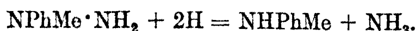
Dilute acetic acid is frequently used with zinc dust. This is the usual method adopted for the reduction of osones to ketoses (*Fischer*) (p. 315):



$$R{\cdot}CO{\cdot}CHO + 2H = R{\cdot}CO{\cdot}CH_2{\cdot}OH.$$

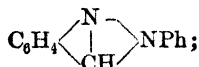
It is also extremely useful in the preparation of hydrazines from nitrosamines and nitramines, *e.g.* *Fischer* (A. 1886, **236**, 198) obtained methyl-phenyl-hydrazine, $NPhMe{\cdot}NH_2$, by the reduction of methyl-phenyl-nitrosamine, $NPhMe{\cdot}NO$. Other reducing agents, *e.g.* metal and concentrated hydrochloric

acid, stannous chloride, zinc dust and alkali, are all liable to carry the reduction a stage further and yield a mixture of ammonia and amine:



$$NPhMe \cdot NH_2 + 2H = NHPhMe + NH_3.$$

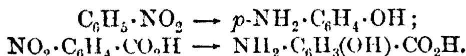
An extremely interesting example of the influence of the reducing agent and the method of reduction on the nature of the final product is met with in the case of nitro-benzyl-phenyl-nitrosamine, $NO_2 \cdot C_6H_4 \cdot CH_2 \cdot NPh \cdot NO$. With tin and hydrochloric acid it yields phenyl-indazole,



with sodium amalgam in alkaline solution, *o*-amino-benzyl-aniline, $NH_2 \cdot C_6H_4 \cdot CH_2 \cdot NHPh$, and ammonia; and with zinc dust and glacial acetic acid, *o*-amino-benzyl-phenyl-hydrazine, $NH_2 \cdot C_6H_4 \cdot CH_2 \cdot NPh \cdot NH_2$. (*Busch*, B. 1894, **27**, 2899.)

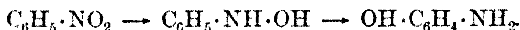
With zinc dust and dilute sulphuric acid the reaction is somewhat slower than with acetic acid; with these reagents sulphonic chlorides may be transformed into thio-phenols, or the reaction may proceed a stage further and the sulphur be completely removed.

Zinc dust and concentrated sulphuric acid are occasionally used for the reduction of nitro-compounds, and in all cases the product is an amino-hydroxy- and not a simple amino-derivative:



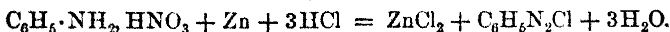
$$C_6H_5 \cdot NO_2 \longrightarrow p\text{-}NH_2 \cdot C_6H_4 \cdot OH;$$
$$NO_2 \cdot C_6H_4 \cdot CO_2H \longrightarrow NH_2 \cdot C_6H_3(OH) \cdot CO_2H.$$

Probably a phenyl-hydroxylamine is first formed, and this then yields the amino-phenol (cf. p. 426):



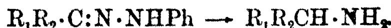
$$C_6H_5 \cdot NO_2 \longrightarrow C_6H_5 \cdot NH \cdot OH \longrightarrow OH \cdot C_6H_4 \cdot NH_2.$$

When zinc or zinc dust and any acid are added to the nitrate of an aromatic amine, a diazonium salt is formed:



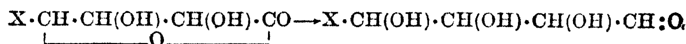
$$C_6H_5 \cdot NH_2, HNO_3 + Zn + 3HCl = ZnCl_2 + C_6H_5N_2Cl + 3H_2O.$$

Sodium amalgam is sometimes used as a reducing agent in the presence of acid; thus with acetic acid it is used for the reduction of hydrazones to primary amines:



$$R_1R_2 \cdot C:N \cdot NHPh \longrightarrow R_1R_2CH \cdot NH_2.$$

Reductions by means of sodium amalgam and dilute sulphuric acid have been largely used by *E. Fischer* in his synthetical work on the sugars, since the lactones of hydroxy-acids when reduced in this way at 0° yield aldoses (pp. 315, 316):



A very common acid reducing agent is hydriodic acid, its reducing action being attributed to the decomposition of the hydrogen iodide into iodine and nascent hydrogen at moderate temperatures. The method was first introduced by *Berthelot*, who, in his earlier experiments, used the acid alone; but when he found that the liberated iodine interfered with the reduction by giving rise to iodo-derivatives or by oxidizing, he added red phosphorus or sometimes phosphonium iodide. The function of the phosphorus is to combine with the iodine immediately it is liberated from the hydrogen iodide, and thus form phosphorus tri-iodide, which is then decomposed by the water present, yielding hydrogen iodide and phosphorous acid. Phosphonium iodide is often formed as a by-product in these reductions. With hydriodic acid alone, practically all oxygen compounds are reduced to saturated hydrocarbons at a temperature of 275°, the reduction being conducted in sealed tubes, *e.g.* glycerol yields propane. Amines are also transformed into paraffins, *e.g.* methylamine yields methane.

When hydriodic acid and phosphorus are used, the reduction can either take place in open vessels, *e.g.* a flask with reflux condenser, or in sealed tubes if a higher temperature is required. As examples of the former we have the following:—$CHI_3 \rightarrow CH_2I_2$; anthraquinone → dihydro-anthracene; benzilic acid, $OH \cdot CPh_2 \cdot CO_2H$ → diphenyl-acetic acid, $CHPh_2 \cdot CO_2H$; tri-hydroxy-glutaric acid, $CO_2H \cdot [CH \cdot OH]_3 \cdot CO_2H$ → glutaric acid; mixed ketones, *e.g.* $C_6H_5 \cdot CO \cdot CH_3$ → hydrocarbons.

As examples of the latter we have the conversion of fatty acids, from $C_8H_{17} \cdot CO_2H$ upwards into paraffin-hydrocarbons, the reduction of anthracene to hydro-anthracenes, and of hydroxy-hexamethylene carboxylic acid, $OH \cdot C_6H_{10} \cdot CO_2H$, to hexahydro-benzoic acid, $C_6H_{11} \cdot CO_2H$.

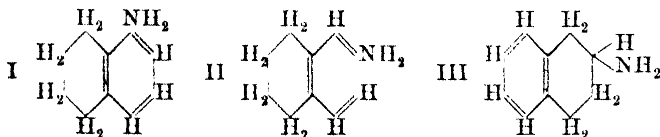
Hydriodic acid is not a good reducing agent for nitro-compounds; as a rule it leaves the nitro-group intact, *e.g.* nitro-benzene-sulphonic chloride, $NO_2 \cdot C_6H_4 \cdot SO_2Cl$, yields first

$NO_2 \cdot C_6H_4 \cdot SO \cdot SO \cdot C_6H_4 \cdot NO_2$, and ultimately *m*-dinitro-diphenyl-disulphide, $NO_2 \cdot C_6H_4 \cdot S \cdot S \cdot C_6H_4 \cdot NO_2$.

Concentrated sulphuric acid and aluminium form a convenient reagent for reducing the CO groups in benzophenone, and anthraquinone to $CH \cdot OH$ groups (M. 1917, **38**, 11).

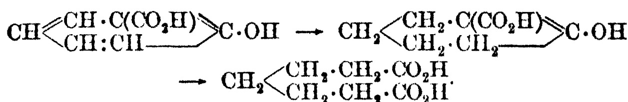
(*b*) **Nascent Hydrogen in Alkaline Solution.** — One of the commonest methods is the addition of metallic sodium, in the form of wire or thin strips, to boiling ethyl alcohol; as a rule it is necessary to use absolute alcohol, as the presence of water diminishes the yields. As examples, we have the reduction of nitriles to primary amines, $R \cdot CN \rightarrow R \cdot CH_2 \cdot NH_2$ (p. 109), of esters to alcohols (p. 75), of naphthalene to dihydro-naphthalene, of pyridine to piperidine (p. 571), although quinoline is not so readily converted by this process into tetrahydro-quinoline, and lastly, of various benzene derivatives, *e.g.* *m*-hydroxy-benzoic acids into corresponding hexahydro-derivatives, *i.e.* derivatives of hexamethylene. When a higher temperature is required than can be attained with ethyl alcohol, boiling amyl alcohol is used (*Bamberger*). By this method naphthalene and its derivatives may be converted into their tetrahydro-compounds, *e.g.* the naphthols, $C_{10}H_7 \cdot OH$, into tetrahydro-naphthols, $C_{10}H_{11} \cdot OH$.

It is interesting to note that the chief reduction product obtained from *α*-naphthylamine is *ar*-tetrahydro-*α*-naphthylamine (I), and from *β*-naphthylamine a mixture of *ar*- and *ac*-tetrahydro-derivatives (II and III):



Similarly phenanthrene is reduced to its tetrahydro-derivative, anthracene to its dihydro-compound, and the benzene carboxylic acids to di-, tetra-, or hexahydro-derivatives, according to the temperature and other conditions of reduction (cf. p. 499); with sodium and boiling amyl alcohol, benzoic acid yields mainly $C_6H_{11} \cdot CO_2H$. In a few cases, when substituted benzoic acids are reduced by this method, a rupture of the ring occurs and an aliphatic acid is formed. One of the best-known examples is the reduction of salicylic acid to pimelic acid (p. 372); in this case it may be assumed that a tetra-

hydro-salicylic acid is first formed, and that by the addition of the elements of water this is converted into pimelic acid:



Although aniline cannot be converted into its hydro-derivatives by this method, aniline-*o*-sulphonic acid yields a hexahydro-derivative. In place of alcohol moist ether is sometimes used in conjunction with sodium. This is generally accomplished by adding the metal to ether floating on water, or better, on a solution of sodium bicarbonate. Dibenzyl ketone can thus be reduced to dibenzyl-carbinol, mesityl oxide to methyl-isobutyl-carbinol, and acid chlorides, $R \cdot COCl$, to the corresponding alcohols, $R \cdot CH_2 \cdot OH$.

Sodium amalgam may be used in place of sodium itself, as a rule in combination with water; the amalgam is added gradually and the mixture kept agitated, and a small amount of alcohol is added, if necessary, to prevent frothing. By this method, benzene and its derivatives may be reduced to di- and tetrahydro-compounds. Many olefine derivatives are reduced to saturated compounds, *e.g.* cinnamic acid, $C_6H_5 \cdot CH:CH. CO_2H$, to phenyl-propionic acid, $C_6H_5 \cdot CH_2 \cdot CH_2 \cdot CO_2H$, and ketones to secondary alcohols. Alcohol is occasionally a better medium than water, and by this method azo- may be reduced to hydrazo-compounds (p. 423), and benzaldehyde and its substituted derivatives into benzyl alcohols.

In many instances the alkali formed by the action of the metal on water or alcohol has a deleterious action on the products of reduction, and it becomes necessary to neutralize the alkali as far as possible. This may be effected by the occasional addition of mineral acid, but is most readily accomplished by *Aschan's* method of leading carbon dioxide through the liquid as the reduction proceeds, and in this way converting the sodium hydroxide into bicarbonate as fast as formed. It is the method often used in the reduction of phthalic acids, &c., and may also be employed for converting naphthalene and resorcinol into their dihydro-derivatives, and benzoic acid into its tetrahydro-compound.

Zinc and alkali are often used to reduce aromatic ketones to secondary alcohols, *e.g.* $(C_6H_5)_2CO \rightarrow (C_6H_5)_2CH \cdot OH$;

whereas when zinc and acetic acid are used, the corresponding pinacones, $(C_6H_5)_2C(OH)\cdot C(OH)(C_6H_5)_2$, are formed. Alkali, especially sodium hydroxide, may be used with zinc dust; the usual method being to keep the alkali and substance well stirred, and to add the zinc dust gradually. As examples we have: Anthraquinone → anthranol; fatty diazo-compounds → hydrazo-compounds; *o*-nitraniline → *o*-phenylene-diamine. Further examples are the dehalogenating of aromatic compounds and the preparation of azoxy- and azo-compounds (p. 425).

(*c*) **Nascent Hydrogen in Neutral Solution.**—Many reductions take place most readily in the absence of free acid or free alkali, and may be effected by the following reagents:—(i) Zinc filings or granulated zinc and alcohol, *e.g.* β-bromo-allo-cinnamic acid → allo-cinnamic acid (p. 484); (ii) *Gladstone-Tribe* couple, in the reduction of alkyl haloids to paraffins (p. 33); (iii) mixture of zinc and iron, in the presence of certain metallic salts, *e.g.* acetone → isopropyl alcohol; (iv) zinc dust and water (or alcohol), which may be used for reducing azo-dyes to mixtures of amines, *e.g.* chrysoidine, $NPh:N\cdot C_6H_3(NH_2)_2$, to aniline and triamino-benzene, and also for reducing aromatic nitro-compounds to the corresponding hydroxylamines, *e.g.* $C_6H_5\cdot NO_2 \rightarrow C_6H_5\cdot NH\cdot OH$, a reaction which proceeds extremely readily in the presence of ammonium chloride solution. The same reagents are extremely useful in converting sulphonic chlorides into sulphinic acids, $C_6H_5\cdot SO_2Cl \rightarrow C_6H_5\cdot SO_2H$. (v) Aluminium amalgam (*Cohen* and *Ormandy*, B.A. Report, 1889, 550) is also a useful neutral reducing agent in the presence of water; by this method nitro-derivatives are readily transformed into hydroxylamines, and ketones to secondary alcohols.

Benzophenone reduced in acid solution gives benzopinacone, $OH\cdot CPh_2\cdot CPh_2\cdot OH$, in alkaline solution benzhydrol, $CPh_2\cdot CH\cdot OH$, and in neutral aqueous solution with aluminium amalgam and alcohol, a mixture of 66 per cent of the latter and 33 of the former.

B. Among other chemical methods we may mention **heating with metals.** Thus azo-benzene is formed when azoxy-benzene is heated with metallic iron, anthracene when alizarin is heated with zinc dust, and pyrrole when succinimide is heated with the same reagent. In all these cases the metal abstracts oxygen and is converted into an oxide. It is a method frequently adopted when dealing with unknown complex sub-

stances and it is desired to know from what simpler compounds they are derived.

Alcohol alone, as in the conversion of diazonium salts into hydrocarbons (p. 415):



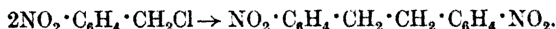
$$C_6H_5N_2Cl + CH_3 \cdot CH_2 \cdot OH = C_6H_6 + N_2 + HCl + CH_3 \cdot CHO.$$

Sodium ethoxide, or often alcoholic potash, for the reduction of nitro-compounds to azoxy- or azo-compounds (*De Bruyn*), and also for reduction of deoxy-benzoin and other aromatic ketones to secondary alcohols, *e.g.* hydroxy-dibenzyl:



$$C_6H_5 \cdot CO \cdot CH_2 \cdot C_6H_5 \rightarrow C_6H_5 \cdot CH(OH) \cdot CH_2 \cdot C_6H_5.$$

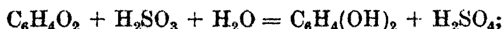
Sodium stannite, obtained by adding an excess of sodium hydroxide to stannous chloride, is employed for preparing azo-compounds from nitrated hydrocarbons, for the reduction of diazonium salts to hydrocarbons, *e.g.* benzene from benzene diazonium chloride. It reduces *p*-nitro-benzyl chloride to dinitro-dibenzyl, the nitro-groups remaining intact:



$$2NO_2 \cdot C_6H_4 \cdot CH_2Cl \rightarrow NO_2 \cdot C_6H_4 \cdot CH_2 \cdot CH_2 \cdot C_6H_4 \cdot NO_2.$$

Hydrogen sulphide, or **ammonium sulphide,** in alcoholic solution (*Cohen* and *M'Candlish*, J. C. S. 1905, 1257, or **pyridine**, 1929, 2264), is made use of for the reduction of nitro- and nitroso-derivatives to amines, and is especially useful when several nitro-groups are present and it is required to reduce only one, *e.g.* m-$C_6H_4(NO_2)_2 \rightarrow m$-$NO_2 \cdot C_6H_4 \cdot NH_2$, $C_6H_2Me(NO_2)_3 \rightarrow NH_2 \cdot C_6H_2Me(NO_2)_2$, &c.; also *o*-nitro-cinnamic acid → α-hydroxy-quinoline or carbostyril (p. 585). In many cases sulphur-derivatives are formed instead of simpler reduction products, especially with ketones or aldehydes.

Sulphurous acid is used in reducing quinones to quinols, *e.g.*



$$C_6H_4O_2 + H_2SO_3 + H_2O = C_6H_4(OH)_2 + H_2SO_4;$$

and **sodium hyposulphite,** $Na_2S_2O_4$, is an extremely useful reagent for preparing leuco-compounds from dyes.

Ferrous sulphate and ammonia form a convenient reducing agent for certain nitro-compounds, *e.g.* nitro-phenylacetic acids.

Phenylhydrazine is a useful agent for reducing δ-trinitro-tri-aminobenzene to hexaminobenzene (J. C. S. 1929, 334).

C. **Catalytic Reduction,** or reduction by means of hydrogen in presence of finely-divided metals. The catalytic action

of finely-divided substances, especially platinum black, in the combination of sulphur dioxide and oxygen, or hydrogen and oxygen, or in the decomposition of hydrogen peroxide, is well known. Similarly many carbon compounds, when mixed with excess of hydrogen and passed over platinum black at a moderate temperature, undergo complete reduction.

The action of finely-divided metals has been investigated (1897–1919) by *Sabatier* and *Senderens*, who find that nickel, cobalt, copper, and iron can act in the same manner as platinum black, and that of these nickel is the most efficient. The metal must be in an extremely fine state of division, and this is accomplished by reducing the metallic oxide in a current of hydrogen at a temperature of about 300°. The substance to be reduced is usually vaporized, mixed with excess of hydrogen, and passed over the metal heated to a temperature which varies somewhat with the different substances, but usually lies between 160° and 250°. A few grams of the metal are usually sufficient and it retains its activity for a long time. The finely-divided metal appears to transform the hydrogen into an active condition comparable with what is usually termed the nascent state. In some cases it is advisable to deposit the nickel on a suitable medium such as infusorial earth, pumice, asbestos, or a membrane. When infusorial earth is used as a support, it is found that in aqueous or aqueous-alcoholic solutions reduction occurs at the ordinary temperature (B. 1916, **49**, 55).

Of the numerous reductions which have been accomplished by this process, we may mention the following:—Carbon monoxide at 200° and carbon dioxide at 300° are reduced to methane and water. Ethylene, propylene, β-hexene, α-octene, &c., are quantitatively reduced to the corresponding paraffins. Acetylene at 150° and α-heptine at 170° yield ethane and heptane respectively. Aromatic hydrocarbons, *e.g.* benzene, toluene, xylene, cymene, at 180° yield their hexahydro-derivatives. Ethyl-benzene reacts in a somewhat curious manner; it appears to be first reduced to its hexahydro-derivative, $C_6H_{11}\cdot C_2H_5$, but this is partially reduced to $C_6H_{11}\cdot CH_3$ and CH_4. Similarly phenyl-acetylene, $C_6H_5\cdot C\vdots CH$, yields a mixture of ethyl-cyclohexane, methyl-cyclohexane, and methane. The terpenes—limonene, sylvestrene, terpinene, menthene—all yield *p*-methyl-isopropyl-cyclohexane. Pinene yields a dihydro-derivative and naphthalene a tetrahydro-compound, and this

with more hydrogen, dekahydro-naphthalene, $C_{18}H_{10}$ (*Leroux*).

Aliphatic nitriles at 180°–200° yield primary amines, and finally secondary and tertiary amines and ammonia:



$$R\cdot CN \rightarrow R\cdot CH_2\cdot NH_2;\ 2R\cdot CH_2\cdot NH_2 \rightarrow (R\cdot CH_2)_2NH + NH_3.$$

Aromatic nitriles yield ammonia and an aromatic hydrocarbon:—$C_6H_5CN + 3H_2 = C_6H_5\cdot CH_3 + NH_3$.

Aromatic chloro-derivatives are readily dehalogenized at temperatures above 270°:—$C_6H_5Cl \rightarrow C_6H_6$, and similarly for polychloro-derivatives. The presence of CH_3, OH, and NH_2 groups appears to facilitate reduction:



$$Cl\cdot C_6H_4\cdot NO_2 \rightarrow C_6H_5\cdot NH_2,\ HCl.$$

Aliphatic nitro-compounds at 150°–180° yield the corresponding primary amines, but at higher temperatures paraffins and ammonia. Aromatic nitro-compounds are best reduced in presence of copper at 300°–400°; in this manner nitrobenzene yields aniline and α-nitro-naphthalene α-naphthylamine and *o*-nitro-phenol *o*-amino-phenol; whereas, when nickel is used, α-nitro-naphthalene yields ammonia and tetrahydronaphthalene.

Phenol, *o*-cresol, thymol, and carvacrol at 170°–180° are reduced to their hexahydro-derivatives, as are also methyl- and ethyl-anilines. Aniline at 190° also yields its hexahydroderivative, cyclohexylamine, $C_6H_{11}\cdot NH_2$, but at the same time dicyclohexylamine, $(C_6H_{11})_2NH$, and cyclohexyl-aniline, $C_6H_{11}\cdot NH\cdot C_6H_5$, are produced. *Schiff's* bases (p. 454) and reduced nickel at 200°–230° give hydrocarbons and secondary amines, *e.g.* $Ph\cdot NH\cdot CH_2Ph$ from benzylideneaniline, together with a little aromatic hydrocarbon (toluene) and base (aniline) (*Maihle*, Bull. Soc., 1919, **25**, 321).

At moderate temperatures (130°–160°) polyhydric phenols yield corresponding hexahydro-derivatives.

Alcohols are formed by the reduction of aldehydes and ketones at temperatures slightly above their boiling-points, *e.g.* $(C_2H_5)_2CO \rightarrow (C_2H_5)_2CH\cdot OH$.

Olefine derivatives are readily transformed into the corresponding saturated compounds at moderate temperatures, and compounds of the aromatic series, *e.g.* cinnamic acid, can be reduced to saturated compounds without the benzene nucleus being effected. Unsaturated ketones, *e.g.* mesityl oxide and phorone, can be reduced to the corresponding saturated

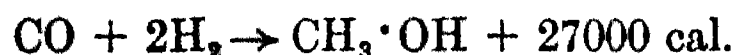
ketones. Diketones yield various products: thus diacetyl at 140°–150° yields a mixture of hydroxyketone and glycol; acetonylacetone yields the anhydride of the corresponding glycol; benzil, benzoin, and benzoylacetone yield the corresponding hydrocarbons. Lævulic acid yields valerolactone, quinones yield quinols and carbylamines, alkyl isocyanates, and oximes yield mixtures of amines, mainly secondary. (*Sabatier* and *Senderens*, Annales, 1905 [viii], **4,** 319; *Sabatier* and *Maihle*, ibid. 1909, **16,** 70; *Sabatier*, B. 1911, **44,** 1984.)

With a slightly active nickel at 300°–350°, ketones of the type benzophenone and phenyl benzyl ketone yield the aromatic hydrocarbons, *e.g.* diphenylmethane and *s*-diphenylethane. With a more active nickel at 170°, the benzene nuclei are also reduced (*Sabatier* and *Murat*, C. R. 1914, **158,** 760).

According to *Boeseken* and *van Senden* (Rec. trav. 1913, **32,** 23), both heptaldehyde and *n*-heptyl alcohol when heated with nickel at 220° yield *n*-hexane together with CO.

Catalytic reduction is now the basis of commercial processes for the manufacture of various organic compounds. The following are some of the more important: A. Vapour Phase: —(1) Methyl alcohol; (2) Hydrogenation of aldehydes and ketones. B. Liquid Phase: (1) Fat hardening; (2) Formation of hexahydro derivatives of phenols, &c.; (3) Reduction of naphthalene.

Methyl alcohol.—The production of methyl alcohol from water gas (cf. p. 77).



$$CO + 2H_2 \rightarrow CH_3 \cdot OH + 27000 \text{ cal.}$$

As the alcohol is required in large quantities in the dye industry for methylating purposes and also for the manufacture of formaldehyde and for use as a solvent, it has been found profitable to manufacture it by this process in order to compete with that from wood distillation factories in France, Germany, and England. The catalyst employed is zinc oxide or preferably granular basic zinc chromate at a temperature of about 400° and a pressure of 150–250 atmospheres. Sulphur compounds must not be present in the gases and traces of iron, nickel or cobalt in the catalyst tend to produce methane. By using an iron alkali catalyst a complex product, **synthol,** is formed; this contains hydrocarbons, alcohols (C_4–C_7), and other oxygenated compounds.

Hydrogenation of aldehydes and ketones by passing hydrogen and the vapour of the compound over a heated nickel catalyst. The nickel is usually obtained by reducing the oxide (from the carbonate or nitrate) with hydrogen at not too high a temperature, frequently the catalyst is used on a porous support, *e.g.* pummice or kieselgühr, impregnated with a nickel salt and then heated and reduced. Such catalysts are more durable and more heat resisting than the metal itself. Ethyl alcohol is manufactured by this process from aldehyde in Switzerland and isopropyl alcohol from acetone in America, as this alcohol is required in perfumery in place of ethyl alcohol. In the latter reaction the optimum temperature is 150–180°, and proceeds best under pressure.

Hardening of Fats.—The process of greatest commercial importance is the hydrogenation of vegetable and fish oils and fats. As already stated (p. 164) the oils of the vegetable and animal kingdom are rich in glycerides of oleic, linolic and linolenic acids, and these on complete reduction yield tristearin. This hydrogenation is accompanied by a rise in the melting-point, a diminution in the iodine value, finally to zero, and a corresponding decrease in the value of the refractive index. The course of the reduction can be readily followed by determining the refractive index of samples from time to time. As a rule complete hydrogenation produces too hard a fat, but by partial hydrogenation it is possible to obtain fats of any consistency suitable for use as butter substitutes (margarine) or as tallow substitutes in the soap and candle industries. The process of hydrogenation is selective, *i.e.* the more unsaturated glycerides are first reduced, *e.g.* all linolein to olein before the latter is attacked. By reduction of linolein it is possible to obtain an iso-olein with the double linkage in position different from what it is in ordinary olein; it has also been proved that during the reduction of olein itself isomeric change can occur and glycerides of elaidic and other isomeric oleic acids can be formed. This has a disadvantage in industry as the salts of these solid oleic acids have not the same lathering power as has sodium oleate and further the crystalline structure of the iso-oleins is different from that of the stearin and thus affect the consistency of the edible fat.

The hydrogen used must be of a high degree of purity in order to avoid poisoning the catalyst. Electrolytic hydrogen is preferable and this can be used when extremely cheap electric

power is available, otherwise water gas and steam over a catalyst consisting of a good oxide of iron ore, Fe_3O_4, containing a little alumina removing the carbon dioxide and monoxide (about 2 per cent) in the product. In addition to the fine nickel powder or nickelized kieselgühr, fine nickel turnings or wool the surface of which has been rendered catalytically active can be used. To activate the surface the metal is immersed in a dilute solution of sodium carbonate and electrolysed at a suitable current density or is steeped in a dilute hypochlorite solution of definite concentration. The metal receives an adhering film of oxide which produces an active catalyst when it is washed, dried, and reduced at about 250°. For review of process for production of hydrogen, of catalysts and of hydrogenation, cf. *Hilditch*, "Catalytic Processes in Applied Chemistry", 1929.

Hydrogenation of Benzene Compounds.—Each molecule of the benzene compound requires six atoms of hydrogen for complete reduction or one ton of phenol requires 25,000 c. ft. of hydrogen. The materials used are usually phenol, and the cresols in a form free from sulphur and tar. The catalyst is nickel, the temperature 160°–200°, usually under a pressure of 4 atmospheres and upwards, with sodium carbonate present as a promoter. The products, sextol, &c. (cf. p. 441) are used as solvents as also their acetyl derivatives. During the reduction of phenol, the Δ^1-tetrahydrophenol is formed which passes over into the ketonic form, viz. ketocyclohexane or sextone. The reduction products boil some 20° lower than the original phenols.

Hydrogenation of Naphthalene takes place at 170–200° under 10–15 atmospheres pressure, but great care has to be taken in the purification of the original hydrocarbon. The products tetrahydro-naphthalene, **tetralin**, b.p. 206–208°, and dekahydro-naphthalene, **dekalin**, b.p. 190–191° are useful solvents. By similar processes menthol can be obtained by reducing thymol and **piperitone**—a terpene ketone, $CMe\begin{matrix}\diagup CH\cdot CO \diagdown \\ \diagdown CH_2\cdot CH_2 \diagup\end{matrix}CH\cdot CHMe_2$, present in oils from many species of eucalyptus, *e.g. E. dives* and *E. piperita* (p. 624), when reduced yield menthone and menthol.

Palladium and Platinum.—These metals can be used either in the finely-divided form, *e.g.* molecular platinum and platinum black, or in the colloidal form.

Fokin (Abs. 1908, ii, 637) determines the **hydrogen value** of unsaturated compounds by ascertaining the volume of hydrogen absorbed by an alcoholic solution of a given weight of the compound when well shaken with the gas in the presence of molecular platinum.

Willstätter and others (B. 1912, **45,** 1471; 1913, **46,** 527; 1918, **51,** 767) have reduced numerous benzene derivatives by means of platinum black and hydrogen, and find that these compounds are not reduced so readily as olefine derivatives; the most convenient method of bringing about the reduction is to shake a glacial acetic acid solution of the aromatic compound with the metal and hydrogen at the atmospheric temperature and pressure. Certain substances, such as sulphur or thiophene, completely prevent reduction. Benzene and its homologues yield hexahydro-derivatives, phenol gives cyclohexanol and cyclohexane, aniline gives ammonia, cyclohexylamine, and dicyclohexylamine. Benzoic acid is more readily reduced than benzene to its hexahydro-derivative, and pyrrole gives pyrrolidine. Naphthalene appears to be immediately reduced to its decahydro-derivative, as the products isolated were always unaltered naphthalene and decahydronaphthalene, whereas dihydronaphthalene when treated in the same manner gives tetrahydronaphthalene with great readiness, and then more slowly the decahydro compound. These results do not support the structure No. III for naphthalene given on p. 528. Extremely interesting results are obtained with the anhydrides of *o*-dicarboxylic acids. With such compounds, *e.g.* phthalic anhydride, it is found to be necessary to open the flask occasionally in order to saturate the metal with oxygen; the reduction then proceeds regularly. Among the first products formed are phthalide (p. 493) and *o*-toluic acid, and finally hexahydrophthalide, hexahydro-*o*-toluic acid, and hexahydrophthalic acid are obtained, indicating that the anhydride ring is reduced more readily than the benzene nucleus. Traces of phthalic anhydride inhibit the reduction of benzene unless the metal is activated by oxygen. Phthalic acid itself is readily reduced in the absence of oxygen, provided no trace of anhydride is present. Indole in the same solvent gives octahydroindole. According to *Hess* (B. 1913, **46,** 3113), the presence of oxygen retards the reduction of pyrrole-derivatives.

For many purposes, *e.g.* reduction of acetylene-derivatives,

platinum is less effective than palladium (*Paal*, B. 1918, **51,** 640).

Colloidal palladium.—*Paal* and *Gerum* (B. 1907, **40,** 2209) show that when hydrogen is passed through an alcoholic solution of nitrobenzene mixed with a small amount of colloidal platinum, a 50-per-cent yield of aniline can be obtained at temperatures between 65° and 85°. They also show (B. 1908, **41,** 2273; 1909, **42,** 1553, 2244, 3930) that unsaturated acids and esters, *e.g.* fumaric acid, maleic acid, cinnamic acid, and methyl cinnamate, can be reduced to their saturated analogues by passing hydrogen into their alcoholic solutions at the ordinary temperature, provided small amounts of colloidal platinum or palladium, or even of palladium black, are present. They have used the method for converting unsaturated oils (oleic acid derivatives) into saturated glycerides. *A. Skita* prepares the colloidal palladium by the addition of *gummi arabicum* to a slightly acidified solution of palladous chloride, and shows that unsaturated ketones are converted into saturated, that citral yields citronellal and citronellol, and that many alkaloids take up hydrogen (B. **42,** 1627; **44,** 2862).

The reduction proceeds most rapidly when the hydrogen is under an increased pressure of 0·25 to 1 atmosphere. (*Skita* and *Ritter*, B. 1910, **43,** 3393.) By this method unsaturated ketones are reduced to saturated without the carbonyl-group being affected:—*d*-pulegone → *d*-menthone, mesityl oxide → methyl-isobutyl ketone. An exception is met with in phorone (p. 143), which yields di-isobutyl carbinol. If, however, a smaller pressure is used, the reduction stops at the formation of the saturated ketone, valerone. Similarly in the other cases, if the pressure of the hydrogen is increased, a saturated secondary alcohol is obtained. Cyclic ketones and aromatic aldehydes can be reduced to alcohols, using a pressure of 5 atmospheres. *Skita* (B. **44,** 2862, and Chem. Zeit., 1911, **35,** 1098) shows that in many cases a solution of palladous chloride in hydrochloric acid can be used, instead of the colloidal metal, with equally good results.

Hydrogen and palladinized charcoal have been used for reducing aminoalkylketones, *e.g.* $R \cdot CO \cdot CH_2 \cdot NH_2$, to the corresponding carbinols, $R \cdot CH(OH) \cdot CH_2 \cdot NH_2$ (Arch. pharm. 1915, **253,** 181), and palladinized barium sulphate and hydrogen reduce acid chlorides to aldehydes (p. 184). Palladium or platinum in a fine state of division, *e.g.* deposited on

barium sulphate, or infusorial earth, reduce unsaturated alcohols, aldehydes of the open chain terpene series to the corresponding saturated analogues without destroying the $CH_2 \cdot OH$, CHO, or CO_2H groups (*Paal*, Chem. Zeit. 1917, ii, 145).

When aromatic alcohols, aldehydes, or ketones are reduced catalytically in acetic acid solution in the presence of colloidal platinum, the products are usually hydrocarbons, *e.g.* benzaldehyde yields toluene and its hexahydro-derivative. If the OH, CHO, or CO groups are protected, then their hexahydro-derivatives are formed, *e.g.* benzylideneaniline gives hexahydrobenzaldehyde, phenylethyl acetate gives β-cyclohexylethyl alcohol, $C_6H_{11} \cdot CH_2 \cdot CH_2 \cdot OH$.

When cinnamaldehyde is reduced in the presence of palladous chloride and gum arabic in aqueous solution, the product is mainly phenylpropaldehyde; with acetic acid as solvent and with $PtCl_4$ and gum arabic, γ-phenylpropyl alcohol is formed; and with more $PtCl_4$, γ-cyclohexylpropyl alcohol.

Hydrogen under High Pressures.—*Ipatieff* (B. **34**, 596, 3579; **35**, 1047, 1057; **36**, 1990, 2003, 2014, 2016; **37**, 2961, 2986; **40**, 1270, 1281, 1827; **41**, 991, 993, 996, 1001; **42**, 2089, 2092, 2097; **45**, 3205, 3218) has studied the reduction by numerous carbon compounds with hydrogen under pressures of 100–120 atmospheres in the presence of various catalysers, more especially nickel and palladium.

A special iron or gun-metal bomb has been constructed for this purpose, and can be heated to the required temperature in an electric furnace. Of the catalytic agents investigated, namely, iron, nickel, copper, aluminium, nickelous and nickelic oxide (Ni_2O_3), the last named was found to be most effective, and only 2–3 grm. were required for 20–30 grm. of the substance to be reduced. The oxide may be used a second time, but afterwards is less active; analysis of the recovered oxide indicates that only a comparatively small amount of reduction to metallic nickel has taken place. In most cases the best temperature is 230°–260°. Under such conditions, acetone yields pure isopropyl-alcohol; acetylacetone, the glycol, $CH_3 \cdot CH(OH) \cdot CH_2 \cdot CH(OH) \cdot CH_3$; phenol, hexahydrophenol; diphenyl, dicyclohexyl; naphthalene, tetra- or dekahydronaphthalene; dibenzyl, dicyclohexylethane; α- and β-naphthols α- and β-dekahydronaphthols, and similarly for sodium β-naphthioate; benzophenone, diphenylmethane; sodium benzoate

sodium hexahydrobenzoate (60 per cent yield of pure acid); aniline, hexahydroaniline (50 per cent yield); diphenylamine, dicyclohexylamine, $(C_6H_{11})_2NH$; quinoline, dekahydroquinoline; anthracene, perhydroanthracene, $C_{14}H_{24}$; phenanthrene, perhydrophenanthrene, $C_{14}H_{24}$; acenaphthene, dekahydroacenaphthene. Olefines are reduced to paraffin derivatives, aqueous solutions of reducing sugars to the corresponding alcohols, and cyclic ketones to the corresponding hydrocarbons.

Ipatieff claims that this method is much better and yields purer products than *Sabatier* and *Senderens'* method (p. 675).

Catalytic dehydrogenation can occur with finely-divided nickel at high temperatures, *e.g.* 350°–360° cyclohexene yields benzene and menthene cymene (*Sabatier* and *Gandion*, C. R. 1919, **168**, 670. Chap. XLIX).

D. **Electrolytic Reduction.**—This reduction is effected by the cathodic hydrogen produced by the electrolysis of aqueous solutions of acids or alkalis. The actual products formed are dependent not merely on the substances reduced, but also upon the conditions: (*a*) nature and concentration of solvent; (*b*) strength of current or the current density; (*c*) the materials of which the electrodes are made, due to the difference of potential at which the hydrogen ions are discharged (as a rule platinum, mercury, or lead electrodes are used); and (*d*) the temperature.

In many cases the reduction is carried out in a double cell provided with a diaphragm. (*a*) The cathode solution is placed in an ordinary unglazed porous cell, and this is introduced into a beaker which serves as the anode compartment; or (*b*) two glazed pots with small perforations are used, and the small annular space between these is packed with asbestos paper. If necessary the liquid can be agitated by using a rotating cathode.

The reduction of nitro-benzene may be cited as one of the best examples which show the effect of conditions on the nature of the product (see table on following page).

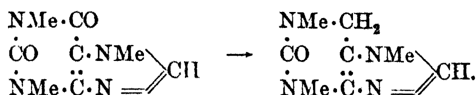
In the reduction of ketonic compounds, *Tafel* (B. 1900, **33**, 2209) has shown that the best effects are obtained by using *pure* lead electrodes, as the hydrogen ions are thus discharged at a higher potential than when other metals are employed, and by employing in the cathode compartment 30–60 per cent sulphuric acid; with stronger acid, reduction of the acid occurs and sulphur is deposited. It is also essential that the current density shall be as low as possible. (For preparation of cells, see *Tafel*.) Acetone when reduced under such con-

NITRO-BENZENE IN THE CATHODE COMPARTMENT

Cathode compartment.	Anode compartment.	Electrodes.	Current density in ampères.	Voltage.	Temperature	Time in ampère hours.	Product.
Alcohol + twice its weight of 25-per-cent sulphuric acid	25-per-cent sulphuric acid	Lead	4–5	3·7–4	65°–80°	35	Aniline and *p*-amino-phenol
Concentrated sulphuric acid + little water	Concentrated sulphuric in porous cell	Platinum	5–6	7–8	75°–80°		*p*-Amino-phenol
3-per-cent sodic hydroxide	15-per-cent sodic sulphate with very little sulphuric acid	Anode lead Cathode nickel	5–6	6–8		22	Azoxy-benzene
70-per-cent ethyl alcohol with sodic acetate	Cold saturated sodic carbonate solution in porous cell	Anode platinum Cathode nickel	6–8	8–9		30	Azo-benzene
70-per-cent ethyl alcohol with sodic acetate	Cold saturated sodic carbonate solution in porous cell	Anode platinum Cathode nickel	First 6–8 then 2–3	8–9		35	Hydrazo-benzene
Concentrated hydrochloric acid	20-per-cent sulphuric acid	Platinum	1·5–2	5–6 5		50	*o*- and *p*-chloranilines

The yield of *p*-amino-phenol can be increased by using a copper cathode and lead in the electrolyte

ditions, using mercury as cathode, yields isopropyl alcohol; but under similar conditions with a lead cathode it yields a mixture of isopropyl alcohol and pinacone. Camphor may be reduced to borneol (p. 635), and caffeine to deoxy-caffeine:



Further, acetanilide, $C_6H_5 \cdot NH \cdot CO \cdot CH_3$, may be reduced to ethyl-aniline, $C_6H_5 \cdot NH \cdot CH_2 \cdot CH_3$; pyridine to piperidine, using lead cathodes; aconitic acid to tricarballylic acid and cinnamic to hydrocinnamic acid, by using mercury cathodes.

The esters of oxalic, malonic, acetoacetic, benzoic, and phthalic acids, when reduced electrolytically, yield ethers, *e.g.*:

Ethyl benzoate ⟶ benzyl-ethyl ether.

E. **Reduction by Micro-organisms.**—Yeast, either in the presence or absence of sugar, can convert acetaldol, $OH \cdot CHMe \cdot CH_2 \cdot CHO$, into β-tutylene glycol, $OH \cdot CHMe \cdot CH_2 \cdot CH_2 \cdot OH$, acetaldehyde to alcohol, and citral into geraniol (*Neuberg*, 1918).

XLV. OXIDATION

Oxidation includes not only those processes in which oxygen is added to a compound, *e.g.* conversion of an aldehyde, R·CH:O, into an acid, R·CO·OH, but also processes in which hydrogen is withdrawn from a compound, *e.g.* transformation of a primary alcohol, $R·CH_2·OH$, into an aldehyde, R·CH:O. In certain cases both processes can occur, *e.g.* oxidation of aniline, $C_6H_5NH_2$, to nitroso-benzene, $C_6H_5·NO$.

Most of the oxidizing agents employed are substances rich in oxygen, *e.g.* potassium dichromate or permanganate, nitric acid, chromic anhydride, peroxides, &c. During the oxidation, although the organic compound is oxidized, the oxidizing substance is reduced, *e.g.* nitric acid gives up part of its oxygen to the substance to be oxidized, and itself becomes reduced to nitrous acid or to various oxides of nitrogen.

Oxygen itself is sometimes made use of as an oxidizing agent, but usually in the presence of a catalyser, *e.g.* finely-divided metals such as platinum black or one of the enzymes known as oxydases. Processes of oxidation, like those of reduction, depend not merely upon the substances to be oxidized, but also on the oxidizing agent selected, and on such conditions as the acid, alkaline, or neutral nature of the solvent, temperature, and concentration. Examples of this have previously been cited among the aromatic hydrocarbons. Thus *m*-xylene is not acted upon by dilute nitric acid, but with chromic anhydride yields isophthalic acid. A very good example is aniline:

Aniline with	Manganese dioxide and sulphuric acid	→ ammonia and little quinone;
	Dichromate mixture	→ quinone;
	Alkaline permanganate	→ azo-benzene and ammonia;
	Acidified permanganate	→ aniline black;
	Neutral permanganate	→ nitro-benzene and azo-benzene;
	Bleaching-powder	→ nitro-benzene;
	Hypochlorous acid	→ *p*-amino-phenol.

Compounds of similar constitution are not always oxidized in the same manner, thus to oxidize *p*-nitro-toluene or *p*-nitro-cinnamic acid the best reagent is dichromate mixture, but for the isomeric *o*-compounds, dilute nitric acid or permanganate are recommended. The inhibiting influence of halogen and

other negative radicals in the *o*-position with regard to the alkyl group, on the oxidation of such hydrocarbons by means of acid oxidizing agents, has already been referred to (p. 467), and also the fact that the final product of oxidation of a benzene homologue depends on the number and positions of the side chains, and not on their length, each yielding ultimately a CO_2H group.

When a compound like cymene, $CH_3 \cdot C_6H_4 \cdot C_3H_7$, is selectively oxidized, it is usually the longer side chain which is first affected; and it has been found possible, in a few cases, to carry the oxidation to a stage where a long side chain has become only partially oxidized, *e.g.* aceto-mesitylene, $C_6H_2Me_3 \cdot CO \cdot CH_3$ to mesityl-glyoxylic acid, $C_6H_2Me_3 \cdot CO \cdot CO_2H$; *m*-butyl toluene, $CH_3 \cdot C_6H_4 \cdot C_4H_9$, by nitric acid at 180°, to *m*-methyl-phenyl-propionic acid, $CH_3 \cdot C_6H_4 \cdot CH_2 \cdot CH_2 \cdot CO_2H$.

Cohen and *Miller* (J. C. S. 1904, **174**, 1622) find that compounds containing chlorine or bromine in the meta-position with regard to a methyl group are least readily oxidized by nitric acid, those with similar substituents in the para-position most readily, and those with *o*-chloro- and bromo-substituents are intermediate.

In certain cases of oxidation, labile groups are present which have to be protected from the oxidizing agent; two such groups are the amino- and aldehydo-groups. An amino- or imino-group can often be protected from undergoing oxidation by transformation into the acetylated group $\cdot$NHAc or :NAc, or even better, into a nitroso-derivative, :N$\cdot$NO. The further oxidation of an aldehydo- to a carboxylic group can often be prevented by the addition of some substance to the oxidizing mixture which will yield a sparingly soluble compound with the aldehyde; such compounds are a primary aryl-amine, which forms a compound of the type of benzylidene-aniline, $C_6H_5 \cdot CH : NC_6H_5$, sodium hydrogen sulphite, or calcium naphthionate, the calcium salt of 1-amino-naphthalene-4-sulphonic acid. From the additive compound to which the last salt gives rise, the aldehyde may be obtained by distillation in steam.

A. Potassium Permanganate.—This is the commonest and one of the most useful oxidizing agents, as it may be used in neutral, alkaline, or acid solution. Other permanganates are also employed, *e.g.* the calcium and barium salts, especially for the oxidation of complex proteins.

(*a*) **Alkaline Solution.**—Even when no alkali is added at the beginning, the solution becomes alkaline during the reaction. The permanganate, a derivative of Mn_2O_7, becomes reduced to hydrated MnO_2, and thus each molecule of permanganate, $K_2Mn_2O_8$, can yield *three* atoms of nascent oxygen:

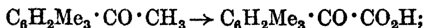


$$K_2Mn_2O_8 + H_2O = 2MnO_2 + 2KOH + 3O.$$

When the product formed is an acid, this remains dissolved in the alkaline liquid, and may often be obtained by the addition of mineral acid after the manganese dioxide has been removed by filtration. In this manner, numerous benzene hydrocarbons and their derivatives can be oxidized to the corresponding acids, *e.g.* *p*-chloro-toluene to *p*-chloro-benzoic acid, naphthalene to phthalonic acid, *o*-$CO_2H \cdot C_6H_4 \cdot CO \cdot CO_2H$. Other examples are the conversion of *o*-nitro-phenol into dinitro-dihydroxy-diphenyl, $NO_2 \cdot (OH)C_6H_3 \cdot C_6H_3(OH) \cdot NO_2$, and of uric acid into allantoin (p. 304).

The oxidation of olefine derivatives by two per cent permanganate (*Fittig*) is of extreme interest. Two hydroxyl groups are invariably added, and a glycol derivative formed; thus cinnamic acid, $C_6H_5 \cdot CH{:}CH \cdot CO_2H$, yields phenyl-glyceric acid, $C_6H_5 \cdot CH(OH) \cdot CH(OH) \cdot CO_2H$. When a stronger permanganate solution or a more powerful oxidizing agent is used, the unsaturated compound is ruptured at the point of the double bond, and a mixture of less complex acids or ketones formed.

An excess of alkali is often added to the permanganate before use. Under these conditions *o*-toluic acid yields phthalic acid, and the method is largely made use of for oxidizing *o*-substituted derivatives of toluene, &c. When the solution is dilute and the temperature is kept at 0°, the oxidation is mild, and can stop at the formation of a glyoxylic acid, *e.g.*:



$$C_6H_2Me_3 \cdot CO \cdot CH_3 \rightarrow C_6H_2Me_3 \cdot CO \cdot CO_2H;$$

otherwise a substituted benzoic acid—in this case $C_6H_2Me_3 \cdot CO_2H$—is always formed. Substituted cinnamic acids, by this method, can be converted into corresponding benzoic acids, *e.g.*:



$$NO_2(OH)C_6H_3 \cdot CH{:}CH \cdot CO_2H \quad \text{to} \quad NO_2(OH)C_6H_3 \cdot CO_2H.$$

Similarly, hydrocarbons of the type of triphenyl-methane,

$CHPh_3$, can be oxidized to carbinols, *e.g.* $CPh_3 \cdot OH$, and compounds of the type of diphenyl-methane, CH_2Ph_2, to ketones, $CPh_2 \cdot CO$.

(*b*) **Neutral Solution.**—In a few cases it is necessary to keep the solution neutral from beginning to end, and this is accomplished by the addition of an excess of magnesium sulphate, which yields insoluble magnesium hydroxide with the caustic potash produced during the oxidation. When acet-*o*-toluidide, $CH_3 \cdot C_6H_4 \cdot NH \cdot CO \cdot CH_3$, is thus oxidized, an 80-per-cent yield of acetanthranilic acid, $CO_2H \cdot C_6H_4 \cdot NH \cdot CO \cdot CH_3$, is formed, whereas in the presence of alkali the yield is only some 30 per cent.

(*c*) **Acid Solution.**—Acetic or sulphuric acid is used, and the acid is added gradually with the permanganate. The method is of use for the preparation of very stable compounds only, as the majority are completely decomposed by these reagents. The reaction is quite different from that in alkaline solution, the permanganate (a derivative of Mn_2O_7) is reduced to a manganous salt (derived from MnO), and thus each molecule of permanganate gives rise to *five* atoms of available oxygen:



$$K_2Mn_2O_8 + 3H_2SO_4 = 2MnSO_4 + K_2SO_4 + 3H_2O + 5O.$$

Sulphides or hydrosulphides in both the aliphatic and aromatic series may be oxidized to sulphonic acids, a reaction which is useful for the preparation of certain naphthalene-sulphonic acids which cannot be obtained by direct sulphonation. *o*-Iodo-benzoic acid may be oxidized to *o*-iodoso-benzoic acid, tetrabromo-*p*-xylene to tetrabromo-terephthalic acid, and primary alcohols to aldehydes.

B. **Chromic Acid Derivatives.—Chromic anhydride,** CrO_3, is often used as an oxidizing agent when dissolved in glacial acetic acid, two molecules of the anhydride yielding three atoms of oxygen, $2CrO_3 = Cr_2O_3 + 3O$. Usually only the theoretical amount required for the oxidation is used, and this is gradually run in from a dropping funnel. Quinoline homologues are oxidized to quinoline-carboxylic acids, and aromatic alcohols to aldehydes, if a primary amine is present to form a *Schiff's* base (p. 454). Even benzene homologues may be oxidized to aldehydes in the presence of acetic anhydride, as the acetyl derivatives thus formed are stable.

Chromyl chloride, CrO_2Cl_2, the chloride of chromic acid, is

used for oxidizing benzene hydrocarbons to aldehydes (*Etard's* reaction, p. 453). The usual method is to dissolve the hydrocarbon and chromyl chloride separately in carbon disulphide, and to run in the chloride solution until the red colour persists, and then to decompose with water. A precipitate of a double compound, *e.g.* $C_6H_5 \cdot CH_3$, $2CrO_2Cl_2$, is first produced, and this is decomposed by water according to the equation:



$$3[C_6H_5CH_3, 2CrO_2Cl_2] = 3C_6H_5CHO + 4CrCl_3 + 2H_2CrO_4 + H_2O.$$

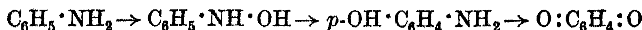
The usual method of using chromic acid is in the form of a mixture of a **dichromate** and **sulphuric acid**, which react according to the equation:



$$K_2Cr_2O_7 + 4H_2SO_4 = K_2SO_4 + Cr_2(SO_4)_3 + 4H_2O + 3O,$$

each molecule of dichromate yielding three atoms of available oxygen. Sometimes potassium dichromate is used, but more frequently the sodium salt, as it is cheaper and more readily soluble in water. As a rule, the dichromate mixture is added gradually to the oxidizable substance. It is the common method of preparing aldehydes from alcohols (p. 128), and also from aromatic hydrocarbons, as there is not the same tendency for the ·CHO group to be further oxidized as when permanganate is employed. Complex alcohols may also be oxidized to ketones or aldehydes, *e.g.* menthol to menthone (p. 623). Many compounds, such as hydroxy-acids, ketones, ketonic acids, &c., are ruptured by chromic acid mixture, and acids or ketones containing a smaller number of carbon atoms are formed.

This is the oxidizing agent usually employed for the preparation of quinones, *e.g.* from aniline, and as a rule the temperature should be kept at about 0°. According to *Bamberger*, the following series of reactions occur:



$$C_6H_5 \cdot NH_2 \rightarrow C_6H_5 \cdot NH \cdot OH \rightarrow p\text{-}OH \cdot C_6H_4 \cdot NH_2 \rightarrow O:C_6H_4:O$$

C. **Nitric Acid.**—Examples of the complete oxidizing action of fuming nitric acid are met with in the ordinary *Carius* method for estimating halogens or sulphur. One of the chief drawbacks of nitric acid is, that in addition to being an oxidizing agent, it is also a nitrating agent, and the products of oxidation, even when dilute acid is used, contain smaller or larger amounts of nitro-derivatives. By means of dilute

nitric acid many benzene homologues are oxidized to carboxylic acids, but the process is slow; thus pentamethyl benzene dissolved in benzene requires sixty hours' boiling to oxidize it to tetramethyl-benzoic acid, and slightly longer time is required to oxidize 2:6-chloro-nitro-toluene to the corresponding acid. An interesting oxidation is that of *m*-butyl-toluene to *m*-methyl-phenyl-propionic acid, and a somewhat complex oxidation is that of camphor to camphoronic acid (p. 632). *Krafft* (B. 1889, **21**, 2735) introduced the use of concentrated nitric acid (sp. gr. 1·5) for oxidizing purposes. The admixture was effected at 0°–10°, the temperature gradually raised to 50°, and the product poured into water. This is a very good method for oxidizing compounds which are already nitrated, as in other cases nitro-derivatives are very liable to be formed. Dinitroxylene is oxidized in this way to dinitrophthalic acid. Sulphoxides, *e.g.* Et_2SO, may be oxidized to sulphones, Et_2SO_2, iodo-benzoic acid to iodoso-benzoic acid, cane-sugar to oxalic acid, &c. The method adopted in oxidizing glycerol to glyceric acid is to allow the aqueous solution of the glycerol to float on concentrated nitric acid.

A mixture of concentrated nitric and sulphuric acids, which is an extremely good nitrating agent, may be used for oxidizing purposes, *e.g.* *o*-nitro-benzyl alcohol to the corresponding aldehyde, of *p*-nitro-cinnamic acid to *p*-nitro-benzaldehyde, and of *s*-trinitro-toluene to *s*-trinitro-benzoic acid.

D. **Sulphuric Acid.**—One of the oldest examples of the oxidizing action of concentrated sulphuric acid is the conversion of ethyl mercaptan, C_2H_5SH, to ethyl disulphide, $(C_2H_5)_2S_2$, and another that of piperidine to pyridine. *Schmidt* introduced the use of fuming sulphuric acid (60 or 70 per cent SO_3) at low temperatures for converting alizarin and other hydroxy-derivatives of anthraquinone into tri- to hexahydroxy-derivatives, many of which are important dyes. The hydroxy-groups form an ester with the sulphuric acid, but this is readily hydrolysed when boiled with dilute acid. Concentrated sulphuric acid may also be used for the preparation of the same compounds, and the yields are largely increased by the addition of boric acid, this being probably due to the fact that boric esters are formed, which prevent the removal of the hydroxy-groups when once introduced.

An oxidizing action of commercial importance is the con-

version of naphthalene into phthalic acid by means of concentrated sulphuric acid and a small amount of mercuric sulphate at a temperature above 300°.

E. **Peroxides.**—The peroxides mainly employed are MnO_2, PbO_2, and occasionally H_2O_2. **Lead peroxide** is frequently used in the form of a paste with acetic acid, one of the earliest oxidations with this reagent being that of uric acid to allantoin (p. 304). Characteristic oxidations are (i) that of α-hydroxy-acids to aldehydo-acids, with one less carbon atom (p. 314), *e.g.*:



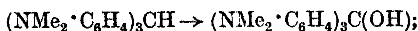
$$CO_2H \cdot CH(OH) \cdot CH_2 \cdot CO_2H \rightarrow CO_2 + O{:}CH \cdot CH_2 \cdot CO_2H;$$

(ii) of alkyl acetates to aldehydes, *e.g.*:



$$o\text{-}NO_2 \cdot C_6H_4 \cdot CH_2 \cdot O \cdot CO \cdot CH_3 \quad \text{to} \quad o\text{-}NO_2 \cdot C_6H_4 \cdot CH{:}O;$$

(iii) of triphenyl-methane-derivatives to the corresponding carbinols, the salts of which are dyes, *e.g.*:



$$(NMe_2 \cdot C_6H_4)_3CH \rightarrow (NMe_2 \cdot C_6H_4)_3C(OH);$$

and (iv) of amino-hydroxy-derivatives of anthraquinone to the corresponding polyhydroxy-derivatives, the NH_2 being replaced by OH, a reaction which does not occur when the amino-group is acetylated. **Manganese dioxide** alone, or in the presence of sulphuric acid, may be used for converting CH_3 groups in benzene homologues into aldehydo-groups. The mixture is kept stirred, and an excess of hydrocarbon is always present. Benzaldehyde, *o*-chloro-benzaldehyde, *p*-nitro-benzaldehyde, terephthalic aldehyde, &c., have been prepared by this method. A remarkable oxidation is that of benzene to benzoic acid by means of the peroxide and sulphuric acid. Hydroxy-acids are often ruptured by these reagents, *e.g.* lactic acid, $CH_3 \cdot CH(OH) \cdot CO_2H$, yields aldehyde and carbonic acid. This is the basis of a method for estimating the strength of solutions of lactic acid by determining the amount of aldehyde formed. The same reagents are also used for the oxidation of alkaloids, and for the conversion of the leuco-bases of triphenyl-methane dyes into the dye salts, *e.g.* *p*-leucaniline into *p*-rosaniline. **Hydrogen peroxide** is often used in the presence of potassium hydroxide for the preparation of organic peroxides, *e.g.* diethyl-peroxide, Et_2O_2, benzoyl-peroxide, $(C_6H_5CO)_2O_2$. Piperidine, when oxidized with three per cent peroxide solution, yields

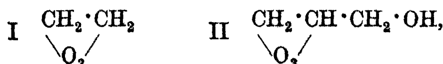
glutaric acid owing to the rupture of the ring. Benzene, with the peroxide, yields a certain amount of phenol. Azo-compounds are converted into corresponding azoxy-derivatives, and phenols into dihydric phenols or quinones. Fatty acids are converted into ketones, $R\cdot CH_2\cdot CO\cdot OH \rightarrow R\cdot CH_2\cdot CO\cdot CH_2R$ (*Dakin*, Am. C. J. 1910, **44**, 41).

Fenton and others (J. C. S. 1894, 899; 1895, 48, 774; 1899, 1) have made use of hydrogen peroxide in the presence of small amounts of ferrous salts; by this method the following reactions have been effected:

Glycollic acid, $OH\cdot CH_2\cdot CO_2H$,	$\rightarrow$	glyoxylic acid, $CHO\cdot CO_2H$;
Lactic acid, $CH_3\cdot CH(OH)\cdot CO_2H$,	$\rightarrow$	pyruvic acid, $CH_3\cdot CO\cdot CO_2H$;
Tartronic acid, $OH\cdot CH(CO_2H)_2$,	$\rightarrow$	mesoxalic acid, $CO(CO_2H)_2$;
Glyceric acid, $OH\cdot CH_2\cdot CH(OH)\cdot CO_2H$,	$\rightarrow$	hydroxy-pyruvic acid, $OH\cdot CH_2\cdot CO\cdot CO_2H$;
Tartaric acid, $CO_2H\cdot CH(OH)\cdot CH(OH)\cdot CO_2H$,	$\rightarrow$	dihydroxy-maleic acid, $CO_2H\cdot C(OH){:}C(OH)\cdot CO_2H$;
Polyhydric alcohols,	$\rightarrow$	aldoses.
Primary amines, $C_6H_5\cdot CH_2\cdot NH_2$	$\rightarrow$	aldehydes, $C_6H_5\cdot CHO$.

F. **Oxygen** itself can often be used for oxidation, generally in the presence of platinum black or platinized asbestos. *Dennsted's* method for estimating carbon and hydrogen in organic compounds is based on this. Many aldehydes, when exposed to moist air, are transformed into acids; thus specimens of benzaldehyde which have been kept for some time contain appreciable amounts of benzoic acid. Cinnamic alcohol may be oxidized to cinnamaldehyde, glycerol to glyceraldehyde, and methyl alcohol to formaldehyde in presence of slightly oxidized copper. Alkaline solutions of polyhydroxylic phenols are readily oxidized (see Pyrogallol), and a similar solution of gallic acid yields the yellow dye galloflavin. *Glock* has shown that methane and air, when repeatedly passed over heated metallic copper at 600°, yield methyl alcohol and formaldehyde, and that ethane and air yield ethyl alcohol, acetaldehyde, and acetic acid. [Compare also *Bone's* experiments (pp. 36 and 37).] Ozone may also be used as an oxidizing agent; it is employed commercially for refining oils, &c. (cf. J. Ind. 1898, 1101). *C. Harries* (A. 1905, **343**, 311; 1910, **374**, 288; 1912, **390**, 235; 1915, **410**, 1) has examined the action of ozone on various types of carbon compounds, mainly in glacial acetic acid solution. Methane, ethyl alcohol, &c., are oxidized to aldehydes and acids, hydrogen peroxide also being formed.

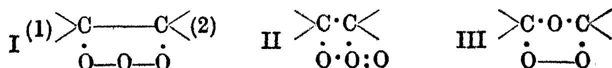
Saturated aldehydes and, to a certain extent, ketones yield labile peroxides of the type, R·CH:O:O. Most unsaturated hydrocarbons and alcohols combine with ozone in suitable solvents, *e.g.* saturated hydrocarbons or alkyl halides,



yielding ozonides, *e.g. ethylene ozonide*, C_2H_4, O_3, I, *allyl alcohol ozonide*, $C_3H_5·OH$, O_3, II, and for each ethylene linking one molecule of ozone is added. Many compounds combine with more than this amount of ozone, yielding **oxozonides,** *e.g.* propyline yields a product, $C_3H_6 + O_4$, which are not readily transformed into normal ozonides. They are regarded as derived from **oxozone,** O_4, which has been shown to be present in ordinary ozone, and hence it is always desirable to purify ozone by passing it through alkali and concentrated sulphuric acid before using it for the preparation of ozonides proper.

After removal of the solvent the ozonides are obtained as oils, syrups, or glassy solids, and in a few cases only as crystalline solids. Some are volatile, but most are extremely unstable, and even highly explosive and hence difficult to prepare. They dissolve in most organic solvents, but tend to decompose in contact with water.

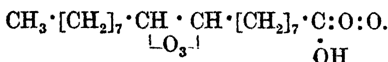
The structure of these compounds suggested by *Harries* is shown in formula I, but more recently *Standinger* (B. 1925, 1088) has suggested that ozonide first formed (molozonide) has the structure indicated by formula II, and that this then polymerizes as in the case of cyclohexene or isomerizes to an iso-ozonide, formula III, *e.g.* ethylene ozonide and to this latter group belong the stable distillable ozonides.



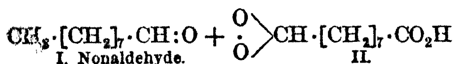
The tendency to polymerization is most marked where the olefine linking is present in a ring structure, acetic acid appears to favour the isomerization to the iso-form, whereas solvents which favour association cause polymerization. If the original olefine compound is not symmetric two isomeric malozonides are theoretically possible.

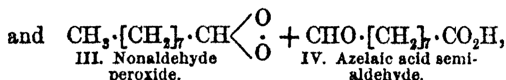
Unsaturated carbonyl derivatives, *e.g.* acids, aldehydes, and

ketones, also combine with ozone, yielding ozonides; they can, however, combine with a fourth atom of oxygen, yielding **perozonides,** which are decomposed by water, yielding the ozonide and hydrogen peroxide. The three atoms of the ozonide are regarded as attached to the two carbon atoms of the ethylene linking, whilst the fourth atom is attached to the carbonyl group. Oleic acid perozonide is represented as:



The ozonides are decomposed when gently heated, or when the solutions in glacial acetic acid are warmed. Oleic acid ozonide decomposes into the four products:





Some of these products are readily oxidized, *e.g.* nonaldehyde yields the corresponding acid, and the semialdehyde yields azelaic. At the same time the aldehyde peroxides are transformed into the isomeric carboxylic acids, so that appreciable amounts of nonylic and azelaic acids are always found in the final decomposition products. The nonaldehyde peroxide formed in this way is isomeric, and not identical with the peroxide obtained by the direct action of ozone on the aldehyde. It is more stable, has m.pt. 73°, and is represented by formula III.

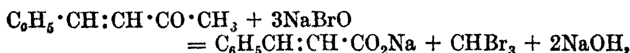
The formation of these products is explicable by either *Harries* or *Standinger's* formula. In the latter case the ozonide in presence of the solvent (acetic acid) yields the iso-ozonide with a rupture between the carbon atoms and this iso-compound then splits up into aldehydes and aldehydeperoxides.

Such decompositions of ozonides, **ozonolysis,** can be used for determining the position of the ethylene linking in the molecule of the original compound, and also for the preparation of certain aldehydes, aldehydic acids, and dialdehydes.

Benzene yields a highly explosive triozonide, $C_6H_6O_9$. With naphthalene one ring adds on ozone more readily than the other, yielding $C_{10}H_8O_6$.

Ozonized oxygen in the presence of concentrated sulphuric acid converts toluene at 100° into benzoic acid.

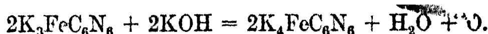
G. **Other Oxidizing Agents.**—**Chlorine** and **bromine** are generally used in alkaline solution, *i.e.* in the form of hypochlorite or hypobromite. As examples, we have the well-known *Hofmann* reaction, the conversion of amides, and imides such as succinimide and phthalimide, into amines or nitriles (pp. 190 and 191); also the oxidation of reduced benzene derivatives back to the original benzene compound. An interesting oxidation is that of benzylidene-acetone to cinnamic acid with four per cent sodium hypobromite:



$$C_6H_5\cdot CH:CH\cdot CO\cdot CH_3 + 3NaBrO = C_6H_5CH:CH\cdot CO_2Na + CHBr_3 + 2NaOH,$$

and of potassium cyanide to cyanate by hypochlorite. Bromine water itself is frequently used for the oxidation of sugars, *e.g.* of an aldose to the corresponding monobasic acid; thus glycerose to glyceric acid, glucose to gluconic acid.

Less common oxidizing agents are **potassium ferricyanide,** which is reduced to the ferrocyanide:



$$2K_3FeC_6N_6 + 2KOH = 2K_4FeC_6N_6 + H_2O + O.$$

s-Trinitro-benzene may be oxidized by this reagent to picric acid, phenyl-acetylene to diphenyl-diacetylene, $CPh \vdots C\cdot C \vdots CPh$, nitroso- to nitro-derivatives, quinone-dioxime to dinitroso-benzene, benzene-diazo-oxides to salts of benzene-diazoic acid, $C_6H_5\cdot N:NO\cdot OH$, and nitro-toluenes to nitro-benzoic acids. **Ferric chloride**:



$$2FeCl_3 + H_2O = 2FeCl_2 + 2HCl + O,$$

may be used for oxidizing hydroxylamine derivatives to nitroso-compounds, *e.g.*:



$$C_6H_4Br\cdot NH\cdot OH \rightarrow C_6H_4Br\cdot NO;$$

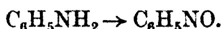
quinols to quinones, and naphthols to dinaphthols:



$$OH\cdot C_{10}H_6\cdot C_{10}H_6\cdot OH.$$

Silver oxide oxidizes glycerol to glycollic acid, and generally aldehydes to acids, and *o*-dihydroxy-benzene to *o*-benzoquinone. In the presence of sodium or ammonium hydroxides silver oxide only oxidizes those compounds containing a

CH·OH or CO group attached to two CH_2·OH, CH·OH, or CO_2H groups or combination of these, *e.g.* tartaric acid, glycerol, and mannitol. In neutral or acid solution it is sufficient if the CH·OH group is combined with CO_2H and with H, CH_2, or CH_3, *e.g.* glycollic, lactic, and malic acids. **Mercuric oxide,** usually with alkali, *e.g.* barium hydroxide, is used for oxidizing fructose to trihydroxy-butyric acid and glycollic acid, and glucose to gluconic acid. It also oxidizes unsym. diethyl-hydrazine to tetraethyl-tetrazone, NEt_2·N:N·NEt_2, and sym. diethyl-hydrazine to mercury-diethyl, nitrogen, and water. **Nitro-benzene** is used as an oxidizing agent in the manufacture of magenta (p. 519), and also in the *Skraup* synthesis of quinoline (p. 582). **Potassium persulphate,** mixed with concentrated sulphuric acid, is known as *Caro's* reagent or sulphomono-per-acid, and can oxidize salicylic acid to 2:5-dihydroxy-benzoic acid, and salicaldehyde to 2:5-dihydroxy-benzaldehyde. It is also used for oxidizing various terpene derivatives, and readily oxidizes aromatic primary amines to nitroso-derivatives, *e.g.*:



$$C_6H_5NH_2 \rightarrow C_6H_5NO.$$

Formaldehyde.—When certain amino alcohols are methylated by means of formaldehyde, it has been found that not merely is the CH_3 group introduced, but at the same time the alcohol is oxidized to an aldehyde or ketone, thus in the case of many cyclic compounds (*Hess*, B. 1913, **46**, 4104; 1915, **48**, 1886),



$$>C(NHR)\cdot CH(OH)— \rightarrow >C(NMeR)\cdot CO—,$$

e.g. 3-α-hydroxy-ethyl-pyrrolidine gives 1-methyl-pyrrolidine-3-acetaldehyde.

H. **Electrolytic Oxidation.**—Organic compounds may be oxidized by means of the oxygen formed at the anode of an electrolytic cell. The method is not so general in application as electrolytic reduction, as it is extremely difficult to stop the reaction at the right point. Even when the theoretical amount of oxygen has been formed, it is often found that part of the compound is unacted on, and part has been completely oxidized. The following are fairly typical examples:—

Purpuro-gallin is formed by the electrolysis of a solution of pyrogallol in sodium sulphate solution, using a rotating platinum anode of 2 sq. dm. The reaction is complete after

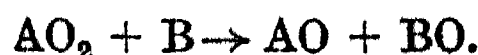
6–8 hours with a C.D. of 1·5–2 ampères and an E.M.F. of 4·3–4·5 volts.

Anthraquinone may be prepared by oxidizing an emulsion of anthracene, water, and sulphuric acid, using a rotating lead cathode, and a leaden vessel as anode. The best yields are obtained when an oxygen carrier, *e.g.* manganese sulphate, is employed with a temperature of 75°–90°, a C.D. of 1–2 ampères, and an E.M.F. of 2·8–3·5 volts.

Numerous azo-dyes have been obtained electrolytically; thus, **Orange II**, or *β-naphthol-azobenzene-sulphonic acid*, $OH \cdot SO_2 \cdot C_6H_4 \cdot N:N \cdot C_{10}H_6 \cdot OH$ (Chap. LV, B.), is produced from an aqueous solution containing sodium sulphanilate, β-naphthol, and sodium nitrite. The cathodes of nickel or platinum wire are placed in two separate cathodic compartments consisting of small porous cells and containing sodium hydroxide solution. The rotating anode is of platinum; and a C.D. of 8–12 ampères, an E.M.F. of 15–18 volts, and as low a temperature as possible, give the best results. The homologues of benzene, when oxidized with platinum electrodes in the presence of sulphuric acid and acetone, yield aldehydes, *e.g.* toluene → benzaldehyde, *o*-xylene → *o*-toluic aldehyde, but the yields, as a rule, are not good. Ortho-substituents of a negative character tend to inhibit such oxidations. Acetic acid solutions of *p*- and *o*-nitro-toluenes yield the corresponding nitro-benzyl alcohols, whereas the *m*-compound yields *m*-nitrobenzaldehyde. Benzyl sulphide yields benzylsulphoxide, benzyldisulphoxide, or tribenzylsulphonium sulphate according to conditions.

I. **Autoxidation.**—Turpentine can absorb oxygen from the air and render it so active that it can oxidize a second substance which normally would not be oxidized in the absence of turpentine. For example air readily bleaches indigo or oxidizes arsenious acid in the presence of turpentine. Other olefine derivatives, *e.g.* amylene, hexylene, fulvene, behave in a similar manner, and it is highly probable that molecular oxygen attaches itself to the olefine linking.

The olefine-oxygen compound is termed the **autoxidator,** and the substance, B, which becomes oxidized, the **acceptor** (*M. Traube*):



$$AO_2 + B \rightarrow AO + BO.$$

The active agent is neither ozone nor hydrogen peroxide, and

in some cases, *e.g.* in the case of pinene, the autoxidator can retain its activity for years if kept in the dark (*Engler*). These compounds are difficult to purify, but a few have been analysed and correspond with a dioxide formula, and dimethyl-fulvene gives a compound $C_8H_{10}O_4$. For recent views especially with reference to autoxidation of ketens (see *Standinger*, B. 1925, 1075).

Benzaldehyde forms an unstable peroxide which is readily isomerized to benzoylhydroperoxide, perbenzoic acid, $C_6H_5 \cdot C \begin{smallmatrix} \nearrow O \\ \searrow O \cdot OH \end{smallmatrix}$ (p. 475), which can act as an autoxidator; it can decolorize indigo, and can oxidize benzaldehyde to benzoic acid. Many autoxidators in the presence of water form hydrogen peroxide: $AO_2 + H_2O \rightarrow AO + H_2O_2$.

Ethylene oxides (p. 198) are also readily formed by the action of benzoylhydroperoxide on olefines.

XLVI. STEREO-CHEMISTRY OF CARBON, SULPHUR, SELENION, TIN, AND NITROGEN COMPOUNDS

A. Carbon Compounds

In preceding chapters (cf. pp. 160, 221, 259) attention has been drawn to the fact that compounds containing a carbon atom attached to four different radicals exist in two optically active isomeric forms and that the isomerism can be attributed to the spatial arrangements of the atoms within the molecule. All natural optically active compounds and all common ones prepared in the laboratory, *e.g.* valeric, lactic, and malic acids, active amyl alcohol, &c., contain two or more carbon atoms. In 1914, *Pope* and *Read* (J. C. S. 1914, 811) succeeded in preparing an optically active compound with only one carbon atom (chloroiodomethanesulphonic acid, CHClI·SO_3H) which is resolved into active forms by fractional precipitation with brucine. Similarly the chlorobromo acid (J. C. S. 1925, 1572).

An extremely interesting conversion of a *d*-compound into its *l*-isomeride without disturbing the attachment of the four atoms directly united to the asymmetric carbon atom has been accomplished by *E. Fischer* and *Brauns* (Abs. 1914, i, 942) in the case of isopropylmalonamic acid. The changes are represented by the following scheme, where Pr represents the isopropyl group:

$$\begin{matrix}H\\Pr\end{matrix}\!>\!C\!<\!\begin{matrix}CO{\cdot}NH_2\\CO{\cdot}OH\end{matrix} \rightarrow \begin{matrix}H\\Pr\end{matrix}\!>\!C\!<\!\begin{matrix}CO{\cdot}NH_2\\CO{\cdot}OMe\end{matrix}$$

$$\rightarrow \begin{matrix}H\\Pr\end{matrix}\!>\!C\!<\!\begin{matrix}CO{\cdot}OH\\CO{\cdot}OMe\end{matrix} \rightarrow \begin{matrix}H\\Pr\end{matrix}\!>\!C\!<\!\begin{matrix}CO{\cdot}OH\\CO{\cdot}NH_2\end{matrix}.$$

The change, $\cdot CO\cdot NH_2 \rightarrow CO\cdot OH$, was effected by means of nitrous acid, and $\cdot CO\cdot OMe \rightarrow \cdot CO\cdot NH_2$ by means of the hydrazidic acid, $CO_2H\cdot CHPr\cdot CO\cdot NH\cdot NH_2$, which gave the azoimide, $CO_2H\cdot CHPr\cdot CON_3$, with nitrous acid, and this with ammonia the amide. The positions of the original $\cdot CO\cdot NH_2$ and $\cdot CO\cdot OH$ groups were thus interchanged, and resulted in an optical inversion.

It has been pointed out already (p. 163) that in a series of derivatives of an active compound, C a, b, c, x, the optical

activity persists * so long as x does not become identical with either a, b, or c. *Fischer* and *Flatau* (Abs. 1909, i. 628) have examined the case of propylisopropylacetic acid in which two of the groups have the same weight, and are similar but not identical. They find that the synthetic acid is readily resolved by means of brucine, and the *d*-acid has $[\alpha]_D = + 11{\cdot}4^\circ$. Propylisopropylcyanoacetic acid also exists in two active forms.

Symmetry and Optical Activity.—In the simple cases already discussed, viz. valeric, lactic, and tartaric acids, the enantiomorphous or nonsuperposable forms, which are the optically active forms, have been characterized by the absence of a plane of symmetry, and the internally compensated forms, *e.g.* mesotartaric acid and mucic acid, by the presence of a *plane of symmetry*. By the term plane of symmetry is understood a plane cutting the figure into two halves, such that the reflection of the one half in a mirror occupying the position of the dividing plane restores the missing half. This is clearly seen in the case of the mesotartaric acid model or projection III, p. 259).

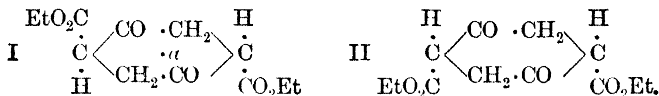
It has been assumed by many chemists that in all cases similar relationships hold good, namely, that the enantiomorphous or optically active forms are always devoid of a plane of symmetry and the superposable forms characterized by the presence of such a plane. This is not correct, as there are many arrangements of atoms which are not enantiomorphous although devoid of a plane of symmetry.

According to *Barker* and *Marsh* (J. C. S. 1913, **103**, 838), the essentials for enantiomorphism, and hence for optical activity, are the absence of (*a*) a plane of symmetry, (*b*) a centre of symmetry, and (*c*) an alternating axis of symmetry.

By *centre of symmetry* is meant a point in the middle of the molecule, such that a line drawn from any atom within the molecule to this point will meet a similar atom when projected in the opposite direction. By rotating the lower halves of the models I, II, and III on p. 259, it will be found that I and II have no such centre of symmetry and that III has. The relationship is seen clearly in the case of certain cyclic com-

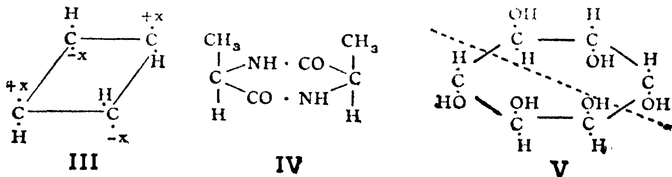
* In some cases racemization may occur in transforming the compound into a derivative, but in such cases the product formed can be resolved into optically active components.

pounds, *e.g.* ethyl succinylosuccinate (p. 501), ethyl trans-2:5-diketocyclohexane-1:4-dicarboxylate (I):



It is clear that a line drawn from any atom (or group) through the point *a* meets a similar atom (or group) on the opposite side of the molecule. The molecule contains a centre of symmetry or is centrosymmetric, and hence does not exist in enantiomorphous forms, and the possibility of optical activity is precluded. The cis compound II, on the other hand, has no such centre of symmetry, and should exist in optically active forms. For the analogous case of 1:4-diketo-2:5-dimethylpiperazins cf. *Fischer*, B. 1906, **39**, 467, 3981.

Alternating axis of symmetry.—This is best illustrated by reference to a tetramethylene compound containing 4 asymmetric carbon atoms attached to the 4 carbon atoms of the ring, viz. $C_4H_4(C\ a, b, c)_4$, where a, b, and c are three different univalent radicals. In two cases these groups, a, b, c, are arranged in the +, and in two cases in the − order. It can be clearly seen by the aid of models that if any one group is rotated through an angle of 90° about the axis vertical to the plane of the 4-carbon ring, and the plane of this ring is regarded as a mirror, the group in question, whether H or C a, b, c, finds its reflection in the corresponding group below. The molecule as such is superposable upon its mirror image; the two are not enantiomorphous, and hence it should be impossible to resolve such a compound into optical isomerides.



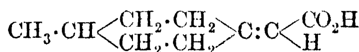
The axis perpendicular to the plane of the ring is termed an alternating axis of symmetry (or sometimes a quaternary mirror axis). This case is quite different from that of the

cis-succinylosuccinic ester (II, p. 702), or the cis-1:4-diketo-2:5-dimethylpiperazin. In the latter case (IV) the two methyl groups are represented in a plane above that containing the piperazine ring, and the two hydrogen atoms in a corresponding plane below. Although the molecule possesses none of the three elements of symmetry already enumerated, it contains an ordinary axis of symmetry, *i.e.* by simply rotating the molecule through 180° about this axis, which is perpendicular to the ring, each atom comes into congruence with a similar atom, and the molecule as a whole presents the same aspect before and after rotation; thus the molecule is not absolutely asymmetric, and yet it is enantiomorphous and its mirror image is not superposable. Two optically active forms should therefore exist, and *E. Fischer* has actually isolated such isomerides. The analogously constituted 2:5-dimethylpiperazine (CH_2 in place of CO) has resisted all attempts to resolve it (J. C. S. 1912, **101,** 2325). An analogous case is that of the optically active isonitols, hexahydroxycyclohexanes (p. 450) (V), where the ordinary axis of symmetry lies in the plane containing the 6 carbon atoms.

Several other types of enantiomorphous carbon compounds are worthy of notice:

(*a*) **Allene** derivatives of the type, $\frac{a}{b}>C:C:C<\frac{a}{b}$. It will be seen by the aid of models that the groups a and b attached to the one carbon atom do not lie in the same plane as the two groups a and b attached to the other terminal carbon atom. The molecule is devoid of any of the elements of symmetry mentioned on p. 701, and should exist in two enantiomorphous, optically active forms. The possibility of such isomerides was pointed out by *van t' Hoff*, but attempts to isolate them have so far not met with success (cf. *Lapworth* and *Wechsler*, J. C. S. 1910, **97,** 38).

(*b*) **1-Methylcyclohexylidene-4-acetic-acid,**

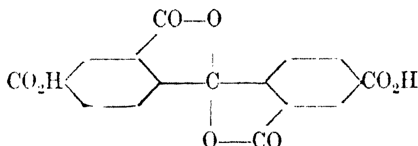


(*Pope, Perkin,* and *Wallach*, J. C. S. 1909, **95,** 1789, cf. ibid. **99,** 1510). This molecule is also devoid of the three elements of symmetry, and exists in enantiomorphous forms. The acid has been resolved by means of brucine into optically active iso-

merides, with m.-pt. 53° and $[\alpha]_D \pm 81°$. It is analogous to the allene derivative mentioned under (*a*), as the C atoms to which the H and CH_3 and the H and COOH groups are attached are rendered incapable of free rotation, the one by ring formation and the other by the olefine linking (cf. p. 252).

An analogous compound is 4-oximino-cyclohexane-1-carboxylic acid, $CO_2H\cdot CH\langle\begin{smallmatrix}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{smallmatrix}\rangle C:N\cdot OH$, which has been resolved by *Mills* and *Bain* (ibid. 1910, **97**, 1866) by means of morphine and quinine. The active sodium salts were obtained, but when acidified with hydrochloric acid an inactive acid was formed. This resolution supports *Hantzsch* and *Werner's* view (p. 711) that when a tervalent nitrogen atom is attached to carbon by a double link the three valencies of the nitrogen atom do not lie in a single plane.

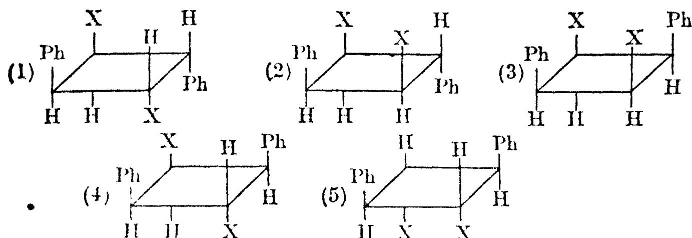
(*c*) Another interesting resolution due to *Mills* and *Nodder* (J. C. S. 1921, 2094), is that of the ketodilactone of benzophenone-2:4:2′:4′ tetracarboxylic acid by means of *l*-α-phenylethylamine,



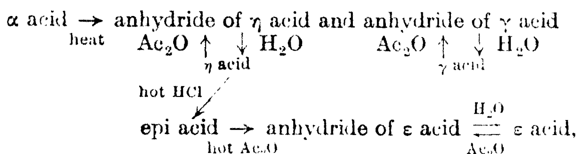
The asymmetry appears to be due to the two halves of the molecule lying in different planes which meet and intersect at right angles at the central carbon atom.

(*d*) The stereochemistry of **cyclobutane** derivatives has received attention, and in the case of the **truxillic acids**, 1:3-diphenylcyclobutane-2:4-dicarboxylic acids, the acids formed from cinnamic acid by additive ring synthesis, all the five possible stereoisomerides, figs. 1 to 5, in which X = CO·OH, have been isolated.

The configurations have been determined by means of (*a*) the formation of anilic acids resolvable into optically active forms (1 and 2), and (*b*) the facility of anhydride formation, *i.e.* the *cis* positions of the carboxyl groups (2, 3 and 5).



The following scheme represents their relationships:



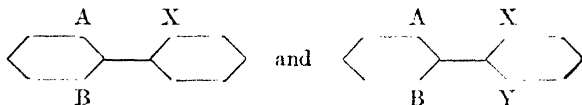
and the α and γ acids give resolvable anilic acid, and hence the structure allocated to the five known acids are $\alpha = 1$, $\gamma = 2$, $\eta = 3$, epi $= 4$ and $\epsilon = 5$.

Stoermer, B. 1923, 676, 1683; 1924, 15; 1925, 2707. Of the six possible **truxinic acids**, 1:2-diphenylcyclobutane-3:4-dicarboxylic acids, also polymers of cinnamic acid, four have been actually isolated.

(*e*) **Diphenyl derivatives.**—As stated in Chap. XXVIII the great majority of diphenyl derivatives can be represented by a uniplanar structure in which the axes of the two rings lie in a straight line, *i.e.* by coaxial and coplanar nuclei. The existence of certain isomerides and the formation of certain complex cyclic derivatives which were used as arguments in favour of a biplanar, *e.g. Kauffler*, formula have been shown to be illusory (*Turner*, J. C. S. 1920, 1140; 1926, 2476; 1927, 2330), and at the present time the only type of diphenyl derivative to which the uniplanar configuration cannot be applied is met with in the 2:6 and 2′:6′-substitution products. Of these the following derivatives of diphenic acid, dibenzyl-2:2′-dicarboxylic acid, have been resolved into optically active components, although each exists in only one *dl*- or racemic form: 6-nitro-, 4:6′-dinitro-, 4:6-dinitro, 6:6′-dichloro-, 6:6′-dinitro-, 6:6′-dimethoxy- (*Kenner* and others, J. C. S.

1921, 593; 1922, 614; 1923, 779, 1948; 1926, 671, 864, 934; 1928, 2340), whereas the following derivatives of diphenyl have resisted all attempts to resolve them: the 2:2'- dicarboxylic acid, 4'-nitro- and 4:4'-dinitro-diphenic acids, the monomethyl ester of diphenic acid, 4-nitro-3:2'-dicarboxylic acid, 4:4'-dinitro-2:3'-dicarboxylic, 4-nitro-2':3-dicarboxylic acid, and 5:5'-dichloro-3:3'-dicarboxylic acid and several other compounds (1928, 1913; A. 1927, **455**, 272; J. A. C. S. 1928, 2499; B. 1929, 2817).

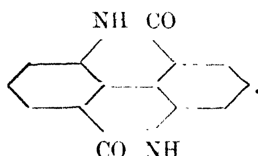
The view generally held (*Turner* and *Le Fevre*, J. Ind. 1926, 831; *Bell* and *Kenyon*, 864; *Mills*, 883, 905) is that in these 6 or 6:6' substituted derivatives of diphenic acid the ortho-substituents tend to push the planes of the rings apart, either by purely mechanical or a combination of mechanical and polar forces, *i.e.* the two nuclei are no longer co-planar and unrestricted free rotation about the common axis is no longer possible, *e.g.* in the case of a 6-nitro-diphenic acid the carboxylic group attached to the second nucleus can pass neither the nitro nor the carboxylic group of the first nucleus and hence an asymmetric structure is formed and *d*- and *l*- isomerides become possible. This steric hindrance is not met with when substituents are in positions 3, 4 or 5. It has been found that the alkaloidal salts of acids such as 4:4'-diphenic acid exist in isomeric forms with activities due to the alkaloid and to an active anion, on liberating the free acid, however, it is found to be inactive. This indicates that in the salt the two benzene nuclei are not coplanar, but become so as soon as the free acid is formed. (J. C. S. 1922, 616; A. 1927, **455**, 272.) If this view is correct then in the types



resolution into active forms should be possible in all cases where A and B are different, and X and Y are different from each other although neither need necessarily be different from A or B. This type of isomerism, which is very similar to that which should exist in allene derivatives, is due to steric hindrance and might possibly be found in other types of compounds. It is possible that the case of maleic acid (p. 252) belongs to this type. Examples might also be met with in the

case of highly substituted acrylic acids, $\frac{A}{B}{>}C{:}C{<}\frac{X}{CO_2H}$ and the isomerism of the two stereoisomeric forms of *l*-triacetyl-β-methylrhamnoside may be due to interference of free rotation in the presence of several substituents (*Haworth* and others, J. C. S. 1929, 2469).

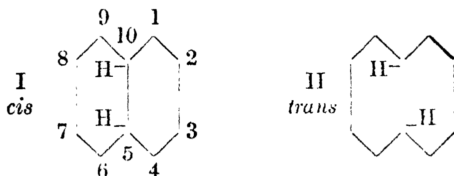
Further resolutions of diphenyl derivatives have been accomplished in the case of 6:6′-diamino-di-*o*-tolyl by means of *d*- or *l*-tartaric acid (*Meisenheimer*, B. 1927, 1425, cf. also J. A. C. S. 1929, 630), but the active bases when acetylated and then oxidized to the corresponding carboxylic acids yield the same inactive lactam,



1:1′-Dinaphthyl-2:2′-dicarboxylic acid, 2:2′-diamino-1:1′-dinaphthyl and similar dinaphthyl derivatives, have been resolved (*Kuhn* and others, A. 1928, **465**, 282; 1929, **470**, 183), and also 8-nitro-1-benzenesulphonylglycinenaphthalene ($\cdot NO_2$ and $\cdot N(SO_2Ph)\cdot CH_2\cdot CO_2H$ in *peri* positions, *Mills* and *Elliott*, J. C. S. 1928, 1291).

(*f*) **Strainless rings.**—It is now clearly established that saturated cyclic structures containing many more than 6 or 7 carbon atoms can exist and that many of them, when once formed, are comparatively stable. It can be shown that the strain in such rings (cf. Chap. XVI) can be relieved when a multiplanar configuration is adopted. In the case of cyclohexane the two possible configurations depicted by *Sachse* (B. 1890, 1363) are:—(*a*) 4 carbon atoms in one plane and the two remaining carbon atoms Nos. 1 and 4 in a second plane (*cis* form); (*b*) 4 carbon atoms in one plane and then Nos. 1 and 4 respectively above and below this plane (*trans* form). Such arrangements necessitate the existence of many isomeric simple substituted derivatives of cyclohexane and as these do not appear to exist, the uniplanar formula for the six carbon atoms is generally accepted. The matter is quite different, however, when condensed polynuclear systems are examined, *e.g.* decahydronaphthalene (*Mohr*, J. pr. 1918 [11] **98**, 315).

Here we may have the 6 carbon atoms, 2, 3, 5, 7, 8 and 10 in one plane, and the atoms 1, 4, 6 and 9 in a second plane, then the two hydrogen atoms attached to Nos. 5 and 10 will both lie on the same side of the six-carbon plane, *e.g.* below, and the second carbon plane (4 atoms) will be on the other side of the six-carbon plane, *e.g.* above; *cis* configuration I. On the other hand, 2, 3, 5, 7, 8 and 10 may form one plane, 1 and 9 a second plane, and 4 and 6 a third plane. Then the H atom attached to No. 10 will be on one side the six-carbon plane and H atom attached to No. 5 will be on the other side. We should therefore have two non-resolvable stereoisomeric decahydronaphthalenes, corresponding with the formulæ I and II,



Such pairs of stereoisomerides have actually been isolated: *cis* and *trans*-hexahydrohomophthalic acid anhydrides (CO in 2 and 4 and O in 3; two 2-ketodecahydronaphthalenes (CO in 2) these are interesting as on oxidation they yield the *cis* and *trans* forms of 1-carboxy-cyclohexane-2-propionic acid (*i.e.* $\cdot CO_2H$ and $\cdot CH_2\cdot CH_2\cdot CO_2H$ in positions 1 and 2 and respectively *cis* and *trans* to one another), and on reduction they yield two isomeric decahydronaphthalenes, which differ by about 8° in boiling point (B. 1924, 683, 1639; A. 1923, **434,** 219); *Kay* and *Stewart* (J. C. S. 1926, 3038) have proved the existence of three out of the four theoretically possible decahydro-2-naphthoamides, they melt respectively at 139°, 165°, and 195°. The four possibilities are:—

(i) $CO\cdot NH_2$ in position 2, *cis* to both H No. 5 and H No. 10.
(ii) $CO\cdot NH_2$ in position 2 *trans* to both H No. 5 and H No. 10.
(iii) $CO\cdot NH_2$ in position 2, *cis* to H No. 5, and *trans* to H No. 10.
(iv) $CO\cdot NH_2$ in position 2, *trans* to H No. 5 and *cis* to H No. 10.

Hückel (A. 1927, **451,** 109) has isolated all four possible 2-hydroxy- and 2-amino-decahydronaphthalenes and has also obtained (ibid., p. 132) 2 *cis* (meso) and 1 *trans* (racemic) form

of hexahydro-β-hydrindol $C_6H_{10}<\begin{smallmatrix}CH_2\\CH_2\end{smallmatrix}>CH\cdot OH$. Compare also *Rao*, J. C. S. 1929, 1951.

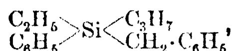
Quinoline can also give rise to a *cis* and *trans* decahydro-derivative (A. 1927, **453,** 163) and similarly tetrahydrocarbazoles (J. C. S. 1927, 2676). *Perkin* and *Sedgwick* (J. C. S. 1924, 2437; 1926, 438, cf. A. 1927, **455,** 171) have obtained 4 optically active tetrahydroacridines. For other cases see J. C. S. 1928, 639, 2583; 1929, 1861, 1975.

For enumeration of the number of isomeric forms of certain hydrogenated polynuclear systems see *Ingold*, Rep. 1924, 94.

An alternative to the multiplanar configuration given above is one in which the two uniplanar cyclohexane rings are inclined at an angle to one another.

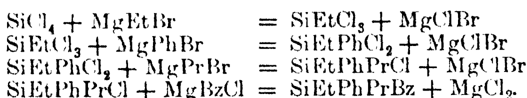
B. Silicon Compounds

Silicon is the element most closely allied to carbon, and hence numerous attempts have been made to prepare optically active silicon compounds containing an asymmetric silicon atom, and in 1907 *Kipping* met with success. (J. C. S. 1907, **91,** 209.) He prepared the compound



$$\begin{matrix}C_2H_5\\C_6H_5\end{matrix}>Si<\begin{matrix}C_3H_7\\CH_2\cdot C_6H_5\end{matrix},$$

ethylpropylbenzylphenylsilicane, by the following series of reactions:—



$$\begin{aligned}SiCl_4 + MgEtBr &= SiEtCl_3 + MgClBr\\ SiEtCl_3 + MgPhBr &= SiEtPhCl_2 + MgClBr\\ SiEtPhCl_2 + MgPrBr &= SiEtPhPrCl + MgClBr\\ SiEtPhPrCl + MgBzCl &= SiEtPhPrBz + MgCl_2.\end{aligned}$$

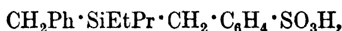
This hydrocarbon when sulphonated gives rise to benzene and a sulphonic acid:



$$SO_3H\cdot C_6H_4\cdot CH_2\cdot SiEtPr\cdot O\cdot SiEtPr\cdot CH_2\cdot C_6H_4\cdot SO_3H,$$

sulphobenzylethylpropylsilicyl oxide. As the formula indicates, this compound contains two similar asymmetric silicon atoms, and should presumably exist in the same number of isomeric modifications as tartaric acid (p. 260). One of the acids isolated by *Kipping* has been shown to be a *d-l*-compound, and its salt with the active base, *d*-methylhydrindamine can be resolved into its optically active components when repeatedly crystallized from acetone or aqueous methyl alcohol.

The two acids have extremely low rotatory powers, *e.g.* $[\alpha]_D$ $\pm$ 3° to 4°. Similar active compounds containing an isobutyl in place of the propyl group have been obtained; they have $[\alpha]_D \pm 10{\cdot}5°$. And still more recently compounds containing a single asymmetric silicon atom have been isolated, *e.g.* **ethylpropyldibenzylsilicanemonosulphonic acid,**



$CH_2Ph{\cdot}SiEtPr{\cdot}CH_2{\cdot}C_6H_4{\cdot}SO_3H$,

which can be resolved into active components by means of brucine. Most of the active silicon derivatives are characterized by the close similarity between the active and racemic forms and by the low rotatory powers, so that it is difficult to say, in certain cases, whether resolution has been effected or not.

Pope and *Peachey* conclude that all the elements of Group IV of the Periodic Classification, namely C, Si, Ti, Ge, Zr, Sn, Ce, Pb, Th, also probably O, S, Se, Te, should in a similar manner give rise to optical activity in their asymmetric derivatives.

Recently **lead** derivatives of the type, Pb, a b, c, d, have been prepared by the following series of reactions:—$PbMe_4 + Br_2$ at $-75° \rightarrow PbMe_3Br + MeBr$; $PbMe_3Br + MgEtBr \rightarrow PbMe_3Et + MgBr_2$; $PbMe_3Et + Br_2 \rightarrow PbMe_2EtBr$; $PbMe_2EtBr + PrMgBr \rightarrow PbMe_2EtPr$, and, finally, a lead compound containing methyl, ethyl, propyl, and butyl groups is obtained. It is worthy of notice that the action of bromine on a mixed lead compound always leads to the elimination of the smallest group, viz. methyl. Further, the four groups may be introduced in different order, but the final product is the same, thus indicating the equivalence of the four valencies. So far the lead compounds have not been resolved into optically active components (*Grüttner* and *Krause*, B. 1917, **50,** 202).

C. Nitrogen Compounds

(*H. O. Jones*, B. A. Rep. 1904, 169)

I. Tervalent Nitrogen Compounds.—No optical activity has been met with in compounds of the type N a, b, c, and all attempts to resolve such compounds have proved fruitless. *Jones* and *Millington* (C. C. 1904, **2,** 952) have attempted to resolve benzyl-phenyl-hydrazine by means of *d*-camphor-sulphonic acid, and to resolve methylethylaniline-sulphonic acid by means of brucine. Other chemists (*Krafft*, *Behrend* and *König*, *Ladenburg*) have attempted to resolve benzyl-ethyl-amine,

p-tolyl-hydrazine, *β*-benzyl-hydroxylamine, methyl-aniline, and tetra-hydroquinoline by means of *d*-tartaric acid.

Kipping and *Salway* (J. C. S. 1904, 438) have adopted the method of treating a secondary amine with a racemic acid chloride, namely *d*-*l*-benzylmethylacetyl chloride, CHMeBz·COCl, and examining the substituted acid amide formed. With a true *d*-*l*-base, the following compounds should be formed: *d*B *d*A, *l*B *l*A, *d*B *l*A, *l*B *d*A, of which 1 and 2 form an enantiomorphously related pair, and 3 and 4 a similar pair. Thus the complete product would be a mixture of two racemic substituted acid amides. Experiments conducted with methyl-aniline, *p*-toluidine, phenyl-hydrazine, and benzyl-aniline gave a homogeneous product in each case. Similarly, when *p*-toluidine and benzyl-aniline are condensed with *d*-methyl-benzylacetyl chloride, no indication of the formation of isomerides is met with.

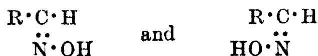
An analogous method, using *d*-hydroxymethylene camphor, $C_8H_{14}\langle\begin{smallmatrix}C:CH\cdot OH\\ \cdot \\ CO\end{smallmatrix}$, which reacts with secondary amines, giving compounds containing the group $:CH\cdot NR^1R^2$ instead of $:CH\cdot OH$, has been used by *Pope* and *Read* (J. C. S. 1909, **95**, 171; 1912, **101**, 2334).

A pair of compounds, $C_6H_3Me_2\cdot NH\cdot CHMe\cdot CH_2\cdot CHO$, containing tervalent nitrogen and stated to be stereoisomeric, have been shown by *Jones* and *White* (J. C. S. 1910, 632) to be structurally isomeric.

The general conclusion to be drawn is, that the centres of gravity of the three radicals, and also of the nitrogen atom itself, lie in a single plane, and the whole arrangement is the most symmetrically possible one.

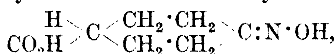
Stereochemistry of Oximes.—The view put forward by *Hantzsch* and *Werner* in 1890 that the pairs of oximes derived from an aldehyde or an unsymmetrical aromatic ketone are stereoisomeric in much the same manner as certain olefine compounds* is still generally supported, although when introduced it was bitterly attacked, and even recently attempts

* The three valencies of the nitrogen atom do not lie in one plane, so that the OH of the :N·OH group can have two different positions giving rise to the two stereoisomerides represented by the projections



have been made by *Atack* (J. C. S. 1921, 1175) to represent such pairs as structurally isomeric, *e.g.* three definite entities, RR′C:N·OH, oxime proper; $RR'C\langle^{NH}_{O}$ iso-oxime, and RR′C:NH:O nitrone.

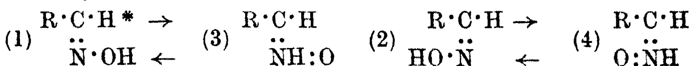
The reasons for retaining the stereochemical formulæ are (1) No purely structural formula can account for the failure to obtain two isomeric oximes from a symmetrical ketone. (2) The stereochemical theory is the only one which will account for the formation of two isomeric methyl ethers, which undoubtedly exist (cf. *Brady* and *Dunn*, J. C. S. 1924, 291). (3) The formation of an optically active oxime (*Mills* and *Bain*, 1910, 1866) of cyclohexanone-4-carboxylic acid,



by the resolution of the synthetic oxime by means of morphine or quinine. For resolution of a phenylhydrazone see J. C. S. 1923, 312.

Such stereochemical formulæ do not admit of the formation of N-ethers which have been proved to exist, and hence the possibility of structural as well as stereo-isomerism must be admitted. The case of the oximes of *p*-nitrobenzophenone has been studied in detail (*Brady* and *Mehta*, 1924, 587). Two oximes are known (*a*) m.p. 158° and (*b*) m.p. 115°, two O-ethers melting at 93° and 96°, and two N-ethers melting at 147° and 176° are also known. Compound (*a*) gives the 90° and 147° ethers, and compound (*b*) the 96°, 147°, and 176° ethers.

It is now generally accepted that the two forms frequently isolated are stereoisomerides 1 and 2, but that each of these can react in tautomeric forms, viz. 3 or 4 which again are stereoisomeric. These latter forms, *nitrone* forms, as a rule cannot be isolated except as ethers. The third structural isomer viz. iso-oxime with a cyclic structure is a mobile tautomeric form of the nitrone or oxime structure (cf. *Plowman* and *Whiteley*, 1924, 587); *Brady* and *Dunn*, 1916, 659; *Griffiths* and *Ingold*, 1925, 1698.



Meisenheimer, *Lange* and *Lamparter*, A. 1925, **444**, 94, have actually isolated four distinct *p*-methoxybenzyl-mon-oximes.

* Or R′.

Determination of Configuration.—The method adopted by *Hantzsch* in the case of aldoximes was to treat the two isomerides with acetyl chloride, the one which readily lost water yielding a nitrile ($\cdot CH:N\cdot OH \rightarrow \cdot C\vdots N$) was given the *syn* or *cis* configuration 1, and the one which yielded a stable acetyl derivative was given the *anti* or *trans* configuration 2.

Again, in the case of stereoisomeric ketoximes an examination was made of the products formed by the *Beckmann* transformation under the influence of acetyl chloride. It was assumed that in this transformation *cis* exchange of groups occurs, *e.g.*:

$$1\quad \begin{matrix} C_6H_5\cdot C\cdot C_6H_4\cdot CH_3 \\ \ddot{N}\cdot OH \end{matrix} \rightarrow \begin{matrix} C_6H_5\cdot C\cdot OH \\ \ddot{N}\cdot C_6H_4\cdot CH_3 \end{matrix} \rightarrow \begin{matrix} C_6H_5\cdot C:O \\ \dot{N}H\cdot C_6H_4\cdot CH_3 \end{matrix}$$

and

$$2\quad \begin{matrix} C_6H_5\cdot C\cdot C_6H_4\cdot CH_3 \\ HO\cdot \ddot{N} \end{matrix} \rightarrow \begin{matrix} HO\cdot C\cdot C_6H_4\cdot CH_3 \\ C_6H_5\dot{N}H \end{matrix} \rightarrow \begin{matrix} CO\cdot C_6H_4\cdot CH_3 \\ C_6H_5\dot{N}H \end{matrix}$$

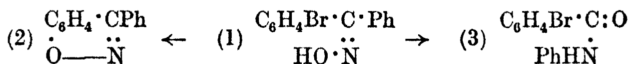
the isomer which yields the toluidide of benzoic acid would have configuration 1, and the one yielding the anilide of toluic acid configuration 2.

Both these methods have been abandoned as reliable tests for configurations. It has been pointed out that they are based entirely on the idea of *cis* elimination and *cis* exchange. It has been proved beyond doubt that frequently in passing from an olefine derivative to an acetylene *trans* elimination occurs (p. 255), and similarly *trans* addition to an acetylene compound often occurs. It is now generally accepted that in nitrile formation from an oxime *trans* elimination takes place, and that in the *Beckmann* transformation *trans* exchange is the rule. This change of view has been largely brought about by a study of the relationships of oximes to cyclic structures, more particularly the benz*iso*oxazoles. *Meisenheimer* (B. 1921, 3206) was able to show that by the fission of tripheny*iso*oxazole (1) with ozone gives a benzoyl derivative of benzil monoxime (2); and the oxime itself (3) subjected to the *Beckmann* rearrangement gives $C_6H_5\cdot NH\cdot CO\cdot CO\cdot C_6H_5$

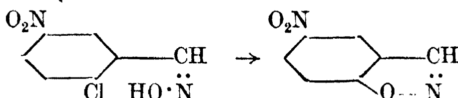
$$(1)\ \begin{matrix} Ph\cdot C\text{——}CPh \\ \ddot{N}\cdot O\cdot \dot{C}Ph \end{matrix} \rightarrow (2)\ \begin{matrix} PhC\cdot COPh \\ \ddot{N}\cdot O\cdot COPh \end{matrix} \rightarrow (3)\ \begin{matrix} Ph\cdot C\cdot COPh \\ \ddot{N}\cdot OH \end{matrix}$$

$$\rightarrow \begin{matrix} HO\cdot C\cdot CO\cdot Ph \\ \ddot{N}Ph \end{matrix} \rightarrow \begin{matrix} PhNH\cdot CO\cdot CO\cdot Ph \\ \cdot \end{matrix}$$

Again, with the *o*-chloro- and *o*-bromo-benzophenone oximes (B. 1924, 289) the compounds (1) which readily lose halogen hydracid yielding benz*iso*oxazole (2) are those which yield anilides of *o*-chloro- and *o*-bromo-benzoic acid (3).

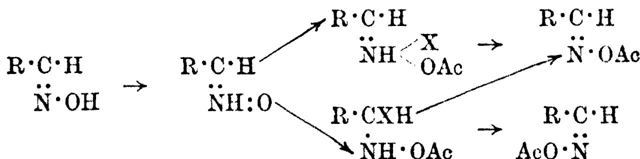


A similar argument can be used in the case of 2-chloro-5-nitrobenzaldoxime, the form



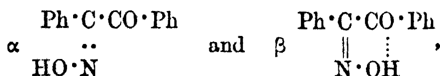
which yields the nitrobenz*iso*oxazole is the one in which H and OH are in *trans* or *anti* positions, *i.e.* the H of the OH and Cl of the benzene ring are vicinal. For examples and discussion, cf. *Brady* and *Bishop*, J. C. S. 1925, 1357; *Beckmann*, *Liesch* and *Correns*, B. 1923, 341; *Auwers* and *Oltens*, 1924, 446).

Brady and *McHugh* (1925, 2414) have examined the interconversion of the geometrical isomerides by acylating 16 aldoximes with 8 different acylating agents, and suggest that the change of configuration of one oxime into the other can be best accounted for by assuming the intervention of the nitrone form and the addition of the acylating agent, *e.g.* $CH_3 \cdot CO \cdot Cl$, to this form in two different ways:—



For conductivities of stereoisomeric oximes see *Brady*, J. C. S. 1929, 946 and for ether formation, 1926, 2403; 1929, 2271.

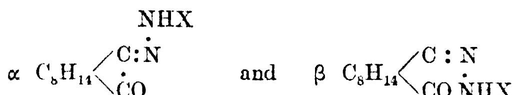
The formulæ,



for the benzil monoximes melting respectively at 134° and 113°

based on the study of isooxazole formation have been recently confirmed by a study of physical properties, *e.g.* solubility and volatility (*Taylor* and *Ewebank*, J. C. S. 1926, 2818). In the β-compound probably a co-ordinate link between O of CO and H of OH (cf. *Sidgwick*, 1925, 907).

The phenylhydrazones derived from unsymmetrical ketones often exist in two forms which are generally regarded as stereoisomeric in the same manner as a pair of oximes, the :N·NHPh replacing the :N·OH grouping. The determination of configuration is again usually based on the ease with which ring closure can occur. The method was first used by *Foster* and *Zimmerli* (J. C. S. 1910, 2156) for camphorquinone phenylhydrazones and semicarbazones:



as the β-compounds, *e.g.* semicarbazone where X = ·CO·NH_2 readily form a cyclic oxytriazine, $C_8H_{14}\left<\begin{array}{l}C:N\cdot NH\\ \dot{C}:N\cdot\dot{C}O\end{array}\right.$.

A similar method has been used in other cases, cf. *Busch* and others, B. 1924, 1783.

(II) **Quinquevalent Nitrogen Compounds.**—(For formation, see pp. 108, 407.) The most interesting type of compound is that in which all five radicals are different, *e.g.* N a, b, c, d, X. These compounds are quaternary ammonium salts, in which four of the radicals are alkyl groups, and the fifth an acid group. No cases of inactive isomerides have been met with. An example described by *Wedekind*, viz. methylallylphenylbenzylammonium iodide, has been shown by *H. O. Jones* (J. C. S. 1905, 1721) to be non-existent.

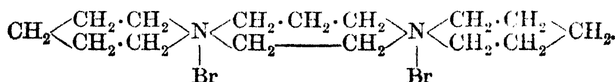
The only known examples of stereoisomerides are the optically active modifications in which compounds of the type **methylethylpropylisobutylammonium chloride,** $N(CH_3)(C_2H_5)(C_3H_7)(C_4H_9)Cl$, exist. This type of compound is always obtained in an inactive form when synthesised in the laboratory by the addition of an alkyl haloid to a tertiary amine. In 1891 *Le Bel* claimed to have obtained a *lævo*-modification by means of *Penicillium glaucum* (green mould), and in 1899 he confirmed this result. In the same year *Pope* and *Peachey* (J. C. S. 1899, 1127) obtained a resolution of *Wede-*

kind's benzylphenylallylmethylammoniumiodide by the aid of silver *d*-camphor-sulphonate.

When the mixture of **benzylphenylallylmethylammonium** *d*-**camphor-sulphonates** is crystallized from acetone, a sparingly soluble fraction is obtained, and this, when treated with potassium iodide, yields an optically active iodide, $N(C_7H_7)(C_6H_5)(C_3H_5)(CH_3)I$, with $[M]_D + 192°$.

H. O. Jones (J. C. S. 1903, 1418; 1904, 223) has resolved phenylbenzylmethylethylammonium iodide and phenylmethylethylallylammonium iodide by means of silver *d*-bromo-camphor-sulphonate. *Jones* has observed that many of these salts show a tendency to undergo racemization, and during the fractional crystallization of the salts it is advisable to keep the temperature as low as possible. Auto-racemization (p. 267) occurs when the cold chloroform solutions are kept in the dark, a phenomenon also observed by *Pope* and *Harvey* (J.C.S. 1901, 828) with other optically active ammonium salts, and probably due to a partial dissociation of the quaternary ammonium salt into tertiary amine and alkyl iodide and subsequent recombination. (For other optically active ammonium salts, see *Wedekind*, B. 1905, **38**, 1838; *Thomas* and *Jones*, J. C. S. 1906, 2[illegible].)

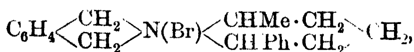
Quinquevalent nitrogen derivatives of the type Na_2bcX,* *e.g.* phenylallyldimethylammonium iodide, phenyldipropylmethylammonium iodide, &c., do not exist in isomeric modifications, and attempts to resolve such compounds into optically active components have given negative results (J. C. S. 1897, 522; 1903, 1141, 1406; 1904, 412). *Aschan* (Zeit. phys. 1903, **46**, 304) has prepared isomeric cyclic nitrogen compounds containing two quinquevalent nitrogen atoms, viz.:



The one compound is formed by the union of ethylene-diperidide with trimethylene bromide, and the other by the combination of trimethylene-diperidide with ethylene bromide. This isomerism can be accounted for if the bromine atoms and the central ring lie in one plane and the other rings in a plane at right angles to the first.

* Compounds of the type aC:N bc X are also non-resolvable (*Wedekind*, A. 1925, **442**, 119).

A similar compound containing one nitrogen atom,

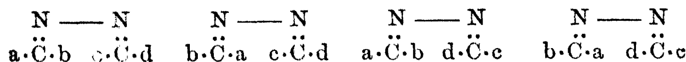


has been shown by *Scholz* (B. **43**, 2121) to exist in two forms.

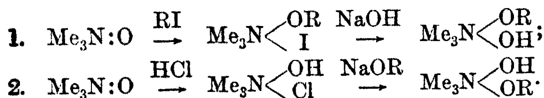
Methylethylaniline oxide, NPhMeEtO, has been resolved into active modifications by means of bromocamphorsulphonic acid. The base itself, probably $NPhMeEt(OH)_2$, has $[\alpha]_D - 25°$ (*Meisenheimer*, A. 1911, **385**, 117).

The compound, $I \cdot NMeEtPh \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot NMeEtPhI$, containing two similar asymmetric nitrogen atoms, like tartaric acid, exists in two inactive forms but so far neither has been resolved into active components. The compound, $I \cdot NMePh(C_3H_5) \cdot CH_2CH_2 \cdot CH_2 \cdot NMePhBz \cdot I$, contains two dissimilar asymmetric nitrogen atoms, and should resemble cinnamic acid dibromide, and exist in two pairs of enantiomorphous compounds. In reality two inactive forms have been isolated, but so far both have resisted all attempts at resolution (*Wedekind*, B. 1910, **43**, 2707; 1916, **49**, 942). When an asymmetric nitrogen atom is introduced into an active compound already containing an asymmetric carbon atom, two active stereoisomerides, which are not optical antipodes, are formed, just as two products are formed when a new asymmetric carbon atom is introduced into an active compound.

An interesting case of the existence of four stereoisomeric compounds of the type, abC:N·N:Ccd, has been demonstrated, viz. with the compound, $CHPh{:}N \cdot N{:}C(SMe) \cdot S \cdot CH_2 \cdot C_6H_4 \cdot NO_2$ (*Busch*, J. pr. 1916, **93**, 25). The four possibilities are:

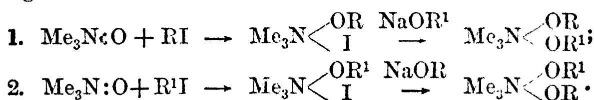


Meisenheimer (A. 1913, **397**, 273) claims to have proved the non-equivalence of the five valencies of the quinquevalent nitrogen atom by the following series of reactions, starting with trimethylamine oxide (p. 114):



As far as could be ascertained, the final products in the two

reactions were not identical but isomeric, as the solution of the first compound when evaporated yielded trimethylamine, an aldehyde, and water, whereas the product from the second series of reactions under similar treatment gave trimethylamine oxide and the alcohol R·OH. In a similar manner isomeric compounds $NMe_3\langle^{OR}_{OR^1}$ have been prepared by the following series of reactions:



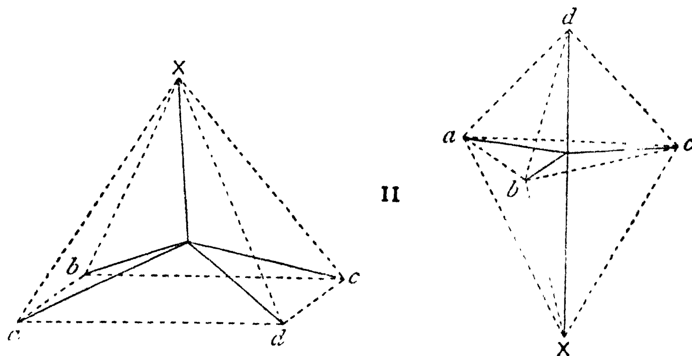
1. $Me_3N{:}O + RI \rightarrow Me_3N\langle^{OR}_{I} \xrightarrow{NaOR^1} Me_3N\langle^{OR}_{OR^1}$;

2. $Me_3N{:}O + R^1I \rightarrow Me_3N\langle^{OR^1}_{I} \xrightarrow{NaOR} Me_3N\langle^{OR^1}_{OR}$.

Compare also A. 1913, **399**, 366, 371, 377.

When three different groups are present in the trialkylamine oxide, it can be resolved into two enantiomorphous, optically active forms by means of tartaric acid.

Various suggestions for the spatial arrangement of the five groups around the quinquevalent nitrogen atom have been made. The one propounded by *Bischoff* represents the nitrogen atom as located at the centre of a pyramid on a rectangular basis and the five groups as situated at the solid angles, the four alkyl groups occupying the basal angles, and the halogen



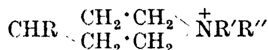
the apex angle (I). Another arrangement suggested by *Willgerodt* represents the nitrogen atom at the centre of a double pyramid on a triangular base, *i.e.* a double tetrahedron configuration (II). The latter arrangement has received but little support owing to the fact that the theoretical number of

isomerides possible with such an arrangement is much greater than the number actually found in practice. Thus two compounds Na_3bX, three compounds Na_2bcX, one of which should exist in optically active forms, and four isomerides NabcdX, all of which should be resolvable.

Within recent years several chemists (*H. O. Jones* and *Dunlop*, J. C. S. 1912, **101**, 1751; *Meisenheimer*, A. 1913, **397**, 300; *Komatsu*, Abs. 1918, i, 426; *Neogi*, J. A. C. S. 1919, **41**, 622) have suggested that the four valencies attaching alkyl groups to nitrogen are distributed in a manner similar to the four valencies in the quadravalent carbon atom, and that the fifth valency occupies quite a different position, *e.g.* is present in an outer sphere or is symmetrically placed with respect to the other four valencies. In reality this is the stereochemistry of the quadravalent substituted ammonium ion $\overset{+}{N}abcd$, and hence the spatial arrangements are similar to those of carbon.

Such a tetrahedral arrangement is in complete harmony with the following results, which have been established by experiment:

1. The non-equivalence of the fifth valency.
2. The non-existence of isomerides of the types Na_3bX and Na_2bcX.
3. The existence of two enantiomorphous isomerides NabcdX.
4. The existence of four active isomerides of the type Cabc·NabcX.
5. The existence of 4-phenyl-1-methyl-1-ethylpiperidonium iodide or generally of salts derived from the ion



in two non-resolvable stereoisomeric (*cis* and *trans*) forms (*Mills, Parkin* and *Ward*, J. C. S. 1927, 2613, cf. 1925, 2507). If the ammonium ion has the tetrahedral configuration the compounds of this type should resemble the cyclohexane-1:4-dicarboxylic acids (Chap. XVI), and exist as *cis* and *trans* isomerides, both of which should be of the non-resolvable type, and this isomerism should disappear in all cases where R′ = R″. On the other hand with a pyramidal configuration of the ammonium ion when R = R′ two non-resolvable forms should exist and when R′ differs from R″ two racemic forms. By an examination of five different compounds of this type,

three in which R′ and R″ were different, and two in which they were identical, it was found that all the facts pointed to the tetrahedral structure.

6. The resolution of the salts amine oxides. These may be represented as containing the ion $\overset{+}{N}abc(OH)$ or in the $\equiv N{:}O$ group the double linking between O and N may be semipolar (*Meisenheimer* and others, A. 1926, **449**, 188).

The discovery of compounds in which nitrogen is attached to five hydrocarbon groups, *e.g.* tetramethylbenzylammonium, $NMe_4{\cdot}CH_2{\cdot}Ph$ (p. 406), does not render the tetrahedral arrangement untenable, as in these compounds one of the five groups appears to occupy a characteristic position with respect to the nitrogen. It has been shown that solutions of such compounds in pyridine are electrolytes, and hence one of the alkyl groups is presumably ionizable as an anion in the same manner as the halogen atom in quaternary ammonium salts.

D. Phosphorus and Arsenic Compounds

Meisenheimer and *Lichtenstadt* (B. 1911, **44**, 356) have obtained methylethylphenylphosphine oxide, O:PMeEtPh, in optically active forms. The base was prepared by combining methyl iodide with ethyldiphenylphosphine, liberating the base with moist silver oxide and then distilling, and was resolved by means of *d*-bromo-camphor-sulphonic acid. The base has $[\alpha]_D + 33{\cdot}8$ in benzene solution. Somewhat similar experiments of *Caven* (J. C. S. 1902, 1362) and *Ephraim* (B. 1911, **44**, 631) have given negative results.

Arsenic compounds, *e.g.* AsMePhαNapI (J. C. S. 1921, 426) and $CO_2H{\cdot}C_6H_4{\cdot}AsMeEtS$ (1925, 2479) have been resolved. For more complex compounds see *M'Cleland* and *Whitworth* (1927, 2753).

E. Sulphur, Selenion and Tin Compounds

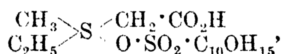
As sulphur, selenion and tin can function as quadravalent elements, *Pope* (1900) examined compounds of these elements in which the central atom is attached to four different monovalent groups in order to ascertain whether such compounds, like their carbon analogues, could not exist in optically active

stereoisomeric forms, and in all cases he and his collaborators met with success.

The sulphur compounds used were derivatives of **methylethylthetine bromide** (*Pope* and *Peachey*, J. C. S. 1900, 1072),

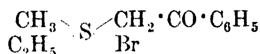


obtained by the addition of bromoacetic acid to methylethyl sulphide. The bromide was mixed with the theoretical amount of silver *d*-camphor-sulphonate in aqueous solution, the silver bromide removed, the filtrate evaporated at 40°, and the solid residue crystallized some 40–50 times from a mixture of absolute alcohol and dry ether. The sparingly soluble *d*-**methylethylthetine** *d*-**camphor-sulphonate,**



melts at 118°–120°, and has a molecular rotation $[M]_D$* = + 68°. The rotation for the camphor-sulphonate ion is + 51·7°, and this gives a rotation of + 16·3° for the thetine ion. A very similar value has been obtained by repeatedly crystallizing the *d*-**bromo-camphor-sulphonate.** The corresponding **platinichloride,** $(SMeEtCl \cdot CH_2 \cdot CO_2H)_2$ $PtCl_4$, has a molecular rotation – 30·2°.

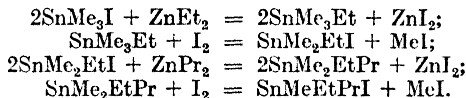
Smiles (J. C. S. 1900, 1174) has obtained **methylethylphenacylsulphine bromide**:



(from methylethyl sulphide and bromo-acetophenone) in optically active modifications by a similar process.

Selenion Compounds have been resolved by *Pope* and *Neville* (J. C. S. 1902, 1552). The compound used was **methylethylselenetine bromide,** $SeMeEtBr \cdot CH_2 \cdot CO_2H$, obtained from methylethyl selenide and bromo-acetic acid; the corresponding *d*-bromo-camphor-sulphonate was repeatedly crystallized from alcohol, and the least soluble fraction melted at 168°, and had $[M]_D$ = + 330·8, which gives a rotation of + 60·8 for the methylethylselenetine ion, and recently **phenyl-*p*-tolyl-methyltelluronium iodide,** $TeMePhC_7H_7I$, has been resolved by similar methods, but the ion is labile and racemises extremely readily (*Lowry* and *Gilbert*, J. C. S. 1929, 2868).

Tin Compounds (*Pope* and *Peachey*, P. 1900, 42, and 116). —A compound containing an asymmetric tin atom was prepared by the following series of reactions:



$$2SnMe_3I + ZnEt_2 = 2SnMe_3Et + ZnI_2;$$
$$SnMe_3Et + I_2 = SnMe_2EtI + MeI;$$
$$2SnMe_2EtI + ZnPr_2 = 2SnMe_2EtPr + ZnI_2;$$
$$SnMe_2EtPr + I_2 = SnMeEtPrI + MeI.$$

The **methylethylpropyl-tin iodide** (a liquid boiling at 270°) was converted into the *d*-camphor-sulphonate by means of silver *d*-camphor-sulphonate, and after the removal of the silver iodide the solution evaporated, when crystals of ***d*-methylethyl-*n*-propyl-tin *d*-camphor-sulphonate,** $SnMeEtPr \cdot O \cdot SO_2 \cdot C_{10}H_{15}O$, melting at 125°–126°, were obtained. In aqueous solution $[M]_D = + 95°$, which gives a value for the univalent ion, SnMeEtPr, of about + 45°. When the mother liquor from the above-mentioned crystals was evaporated, a further quantity of the same compound was obtained, and the operation repeated until all the water has been expelled. No trace of *l*-methylethylpropyl-tin *d*-camphor-sulphonate could be isolated. *Pope* and *Peachey* attribute this to the conversion of the *l*-base into the *d*-base by continued racemization (p. 266), in the following manner:—The solution of the racemic base with the *d*-acid deposits a portion of its *d*-base as the sparingly soluble salt *d*-base + *d*-acid; the excess of *l*- over *d*-base remaining in the solution racemizes as evaporation proceeds, a further quantity of *d*-base separates as salt, and racemization of the residue again proceeds.

A *d*-methylethyl-*n*-propyl-tin iodide with $[\alpha]_D + 23°$ in ethereal solution has been prepared from the camphor-sulphonate.

The resolution of tin compounds has also been accomplished by means of the *d*-bromo-camphor-sulphonate. If the aqueous solution of *d*-methylethyl-*n*-propyl-tin d-bromo-camphor-sulphonate is heated at 100° in a sealed tube for two hours, racemization proceeds, and the rotation $[M]_D + 272°$ is that due to bromo-camphor-sulphonate ion only.

The formation of these optically active compounds was supposed to indicate that the four groups attached to the central S, Se or Sn atom are arranged tetrahedrally around the atom as in the corresponding carbon compounds. The detailed study of the quinquevalent nitrogen compounds and the con-

clusion that the optical activity of these is due to the ion $\overset{+}{N}abcd$, led to the view that in the optically active S, Se and Sn compounds, which are all salts and contain an ionizing atom or group attached to the central atom, the activity is due to a cation in which S, Se or Sn is attached to three different groups, *e.g.* the **thionium** or **sulphonium** ion, $\overset{+}{S}MeEt\cdot CH_2\cdot CO_2H$ in the sulphur compounds, as the ionizing group or atom, *e.g.* Br or I can be neglected in stereochemical considerations.

It is now more or less generally accepted that the arrangement in such ions is that the central S atom itself and the three groups occupy the corners of a tetrahedron. Thus the compound Nabc and the ion $\overset{+}{S}abc$ are spatially quite different.

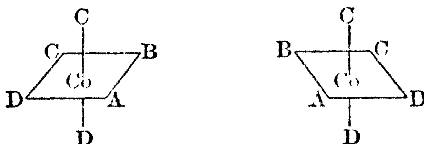
Just as the amine oxides Nabc:O or $\overset{+}{N}abc\cdot OH$ exist in enantiomorphous forms, so do the sulphoxides O:SRR′ (*Harrison, Kenyon*, and *Phillips*, J. C. S. 1926, 2079), and sulphinates $R\cdot S\!<\!{}^{O}_{OEt}$ (*Phillips*, J. C. S. 1925, 2552). The existence of such stereoisomerides is not explicable with the usual structural formula, but adopting *Lowry's* view (J. C. S. 1923, 822) of a semipolar double bond, *i.e.* one of the two linkings, an ordinary C·C or covalency linkage and the other an ionizing one, cf. Chap. XLVIII, F, we have the formulæ $\overset{-}{O}\cdot\overset{+}{S}\!<\!{}^{R}_{R}$ and $\overset{-}{O}\cdot\overset{+}{S}\!<\!{}^{R}_{OEt}$ respectively for sulphoxides and ethyl sulphinates, *i.e.* the attachment of a sulphur atom by three single linkings to three different groups, in other words the arrangement in the optically active thionium ion described above. The compounds actually resolved were *p*-toluene sulphinate, *p*-tolyl-*p*-aminophenyl sulphoxide and *m*-carboxyphenylmethyl sulphoxide and still later a sulphilimine, $C_6H_4\cdot SO_2\cdot\overset{-}{N}-\overset{+}{S}\!<\!{}^{C_6H_4CO_2H}_{CH_3}$, obtained by condensing chloramine T with *m*-carboxyphenyl methyl sulphide (J. C. S. 1927, 188), by means of brucine or cinchonidine. Optical activity disappears when the active sulphinates and sulphoxides are oxidized respectively to sulphonates and sulphones.

Disulphoxides of the cyclic type $O:S\!<\!{}^{CH_2\cdot CH_2}_{CH_2\cdot CH_2}\!>\!S:O$ exist in two inactive stereoisomeric forms (*Bell* and *Bennett*, J. C. S.

1927, 1798; 1928, 86), which can be accounted for on the semipolar double bond basis, thus each S atom carries a + and each O a − charge and the two oxygen atoms can be *cis* or *trans* to the plane of the carbon and sulphur atoms, and also oxides of the type $O:S\langle\begin{smallmatrix}CH_2\cdot CH_2\\CH_2\cdot CH_2\end{smallmatrix}\rangle Cab$ (J. C. S. 1929, 2832; 1930, 1).

F. Co-ordinated Complex Salts

In 1911 *Werner* (B. 1911, 1887, 2445, 3722, 3279) obtained complex optically active derivatives of cobalt. *Werner* pointed out that compounds like CoA_3BCD, $CoABC_2D_2$, or $CoABC_4$ should exist in optically active isomerides, provided the cobalt atoms occupy the centre of an octahedron and the six radicals are situated at the solid angles, *e.g.*:



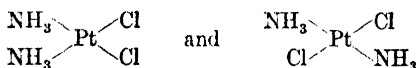
Such active isomerides have been isolated in the case of 1-chloro(or bromo)-2-ammine-diethylenediamine-cobaltic salts, $[CoBrNH_3en_2]Br_2$, where C_2 and D_2 are replaced by divalent ethylenediamine radicals ($NH_2\cdot CH_2\cdot CH_2\cdot NH_2$:). The resolution was effected by means of *d*-bromocamphorsulphonic acid, and the active salts obtained were quite stable. Similar cases of isomerism have been met with in the case of chromium derivatives (*Werner*, ibid. 3132, cf. also A. **386**, 1).

In the spatial arrangement only the non-ionizable groups within the brackets [ ] are taken into account. The anions, whether in solution or in the solid, are quite separate and do not affect the spatial grouping of the other radicals.

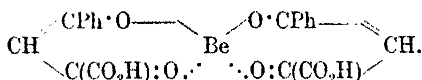
In the above cobalt compounds, when an unsymmetrical diamine, *e.g.* $NH_2\cdot CH_2\cdot CHR\cdot NH_2$, takes the place of DD, a sym. diamine the place of CC, and A = B, two series of compounds exist, α and β (Helv. Chim. 1919, **1**, 5).

The following elements give 6-co-ordination compounds of the octahedral type, viz. Cr, Fe, Ru, Rh, Ir and Pt. For a non-ionizable compound see isomeric tetramethyl ferrocyanides

$Fe(CN)_2(CNCH_3)_4$ (J. C. S. 1930, 321), and for the arsenic compound $[As(C_6H_4O_2)_3]H, 5H_2O$, cf. B. 1925, 2000. In the case of 4-coordination compounds some, *e.g.* $PtCl_2, 2NH_3$, appear to have a uniplanar structure



as two isomerides are known (J. A. C. S. 1922, 2404), whereas others have a tetrahedral configuration, *e.g.* beryllium-benzoyl pyruvic acid and the corresponding zinc and copper compounds (*Mills* and *Gotts*, J. C. S. 1926, 3121) as these exist in two optically active forms indicating a tetrahedral arrangement of the 4 valencies (2 covalent and 2 residual) around the central metallic atom



For nickel compounds cf. *Mann*, J. C. S. 1927, 2904, for some cobalt compounds, *Briggs*, 1919, 67; 1929, 685, 1317, 1505; and copper compounds *Riley*, 1928, 2985; 1929, 1307.

XLVII. RELATIONSHIPS BETWEEN PHYSICAL PROPERTIES AND CHEMICAL CONSTITUTION

A. Boiling-point

Attention has been repeatedly drawn to the fact that in any homologous series the boiling-point tends to increase with the number of carbon atoms present (see pp. 30, 70, 146).

In the majority of cases the increase in boiling-point for each additional CH_2 is not constant, but tends to decrease with increasing molecular weight (*e.g.* fatty acids, and especially the paraffin hydrocarbons and alkyl haloids).

In the case of the ethyl esters of the normal fatty acids the increase is fairly constant, and is about 21° for a CH_2 group (*Kopp*, 1842), *e.g.*:

		Difference.
Ethyl formate	54·5°	
		→ 22·5°
Ethyl acetate	77°	
		→ 21°
Ethyl propionate	98°	
		→ 22°
Ethyl butyrate	120°	
		→ 24·5°
Ethyl valerate	144·5°	
		→ 22·5°
Ethyl hexoate	167°	
		→ 21°
Ethyl heptoate	188°	
		→ 20°
Ethyl octoate	208°	
		→ 20°
Ethyl nonoate	228°	

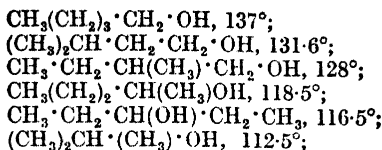
With the alkyl chlorides the difference between methyl and ethyl chlorides is 35°, and this difference diminishes by 2° for each subsequent homologue, so that the difference between heptyl and octyl chlorides is only 23° (*Schorlemmer*).

Attempts have been made to find a general law for the diminution of the difference in boiling-point with increase in molecular complexity. *Goldstein* suggested the formula

$$\frac{n-1}{n}380 + (n-1)\,19 - 340{\cdot}9°$$

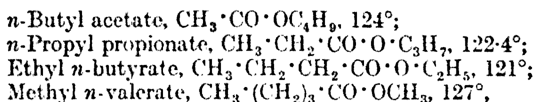
for the boiling-points of the normal hydrocarbons, where n = the number of carbon atoms; this gives good results up to $C_{12}H_{26}$, but not beyond. (Compare also *Mills*, Phil. Mag. [5], **17**, 180.)

A comparison of isomeric substances shows that the boiling-points can vary considerably, even when the isomerides belong to the same series, *e.g.* the amyl alcohols:


$CH_3(CH_2)_3{\cdot}CH_2{\cdot}OH$, 137°;
$(CH_3)_2CH{\cdot}CH_2{\cdot}CH_2{\cdot}OH$, 131·6°;
$CH_3{\cdot}CH_2{\cdot}CH(CH_3){\cdot}CH_2{\cdot}OH$, 128°;
$CH_3(CH_2)_2{\cdot}CH(CH_3)OH$, 118·5°;
$CH_3{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2{\cdot}CH_3$, 116·5°;
$(CH_3)_2CH{\cdot}(CH_3){\cdot}OH$, 112·5°;

In all such cases the normal compound has the highest boiling-point, and the more branched the carbon chain becomes, the lower is the boiling-point. Generally there is a difference of 7° between the boiling-points of a pair of isomeric compounds of the type $CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}X$ and $(CH_3)_2{\cdot}CH{\cdot}X$. According to *Menschutkin*, in a group of isomeric alcohols, amines, or amides, the boiling-point falls as the side chain approaches the hydroxy- or amino-substituent.

A comparison of isomeric esters, *e.g.*:


n-Butyl acetate, $CH_3{\cdot}CO{\cdot}OC_4H_9$, 124°;
n-Propyl propionate, $CH_3{\cdot}CH_2{\cdot}CO{\cdot}O{\cdot}C_3H_7$, 122·4°;
Ethyl *n*-butyrate, $CH_3{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}O{\cdot}C_2H_5$, 121°;
Methyl *n*-valerate, $CH_3{\cdot}(CH_2)_3{\cdot}CO{\cdot}OCH_3$, 127°,

shows that the boiling-point is lower the nearer the oxygen atoms are to the middle of the carbon chain.

A remarkable feature is the relatively high boiling-points of hydroxylic compounds when compared with their isomerides or with closely related compounds. As an example, the *n*-acid isomeric with the last-mentioned group of esters, namely *n*-hexoic acid, boils at 205°. A similar relationship can be shown by the comparison of an alcohol with the ethers isomeric with it. Similarly, a comparison of the boiling-points of the ethyl-derivatives, C_2H_6, $C_2H_5{\cdot}OH$, C_2H_5Cl, C_2H_5Br, $C_2H_5NH_2$, $C_2H_5{\cdot}OEt$, $C_2H_5{\cdot}CN$, indicates the enormous effect of the hydroxyl group on the boiling-point, or, again, a comparison of the boiling-point of an acid with those of its chloride, esters, anhydride, or nitrile.

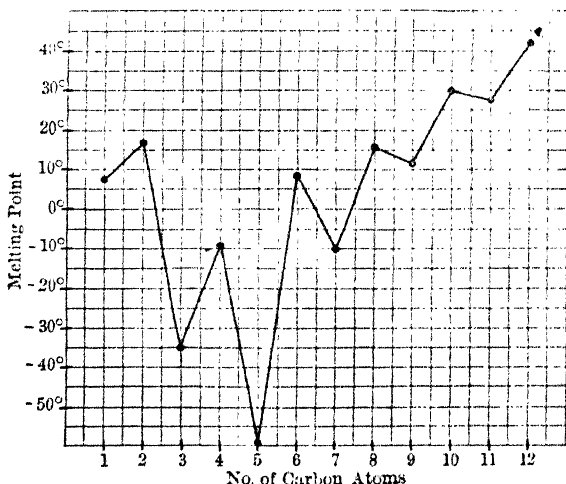
The effect of the introduction of halogen atoms has already been referred to (p. 57). The introduction of an atom of chlorine for hydrogen often raises the boiling-point some 60°, an atom of bromine about 84°, and an atom of iodine 110°; and the introduction of a second or third chlorine atom further raises the boiling-point, but not to the same extent.

Extremely interesting is the fact that a saturated compound and its ethylene analogue have very nearly the same boiling-

points (cf. propyl and allyl alcohols, both 97°; C_7H_{16} and C_7H_{14}, both 99°; propionic acid, 140·7°; and acrylic acid, 140°), although they differ considerably as regards most of their other physical characteristics. Further, methyl ketones, acetyl esters, and corresponding acid chlorides boil at very nearly the same temperature, *e.g.* acetone, methyl acetate, and acetyl chloride at 55°–56°; propyl methyl ketone, methyl butyrate, and butyryl chloride at 101°–105° (*Schröder*, *B.* 1883, **16**, 1312).

B. Melting-point

Although, on the whole, in any homologous series the melting-points of the solid members tend to rise with increase in molecular complexity, in many series an alternating rise and fall is met with, the members containing an even number of carbon atoms melting at relatively higher temperatures than those with an odd number. This is the case with the higher fatty acids, as is readily seen when the melting-points

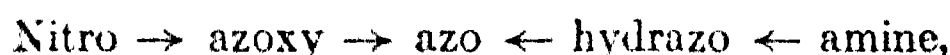


are plotted against the number of carbon atoms. Many other series show a similar relationship, *e.g.* dibasic acids

C_4, 180°; C_5, 97°; C_6, 148°; C_7, 103°; C_8, 140°; C_9, 106°; C_{10}, 127°.

(Compare also *Beach*, Zeit. phys. 1904, **50,** 43.) For amides, cf. J. C. S. 1908, 1033; 1919, 1210; 1927, 2926. In the case of a group of closely related isomeric compounds it is found that the melting-point tends to rise with the number of side chains or branches, *e.g.* $CH_3 \cdot CH_2 \cdot CH_2 \cdot CH_2 \cdot OH$ is a liquid, and $C(CH_3)_3 \cdot OH$ melts at 25°; or again, glutaric acid melts at 97°, methyl-succinic at 112°, and dimethyl-malonic at 117°. The conversion of an acid into an ester always produces a lowering of the melting-point, and the methyl ester always has the highest melting-point of any of the esters derived from a given acid; in fact, in many cases the methyl esters are solids, and the ethyl and higher esters liquids at the ordinary temperature.

In the aromatic series the *p*-compound has a higher melting-point than the *o* and *m* isomerides. With a pair of isomerides the higher melting is always the more stable compound. *G. Schultz* (A. 1881, **207,** 362) has shown that in the group of compounds,


Nitro → azoxy → azo ← hydrazo ← amine,

the melting-point increases up to the azo-compound, and then falls again to the amine. According to *Franchimont* (Rec. 1897, **16,** 126), the melting-point of an organic compound is invariably raised when two hydrogen atoms attached to the same carbon are replaced by oxygen, or when a hydrogen atom is replaced by hydroxyl; cf. $C_6H_5 \cdot CH_2 \cdot OH$ and $C_6H_5 \cdot CO \cdot OH$, or C_6H_6 and $C_6H_5 \cdot OH$.

C. Molecular Volume

The relationships between specific gravity and chemical constitution are not so marked as in the case of other physical properties. Attention has already been drawn to the fact that in a homologous series the specific gravity either decreases with an increase in the number of carbon atoms, and tends to reach a minimum value (p. 146), or increases with the number of carbon atoms and tends to attain a maximum (p. 30).

More interesting results have been obtained by an examination of molecular volumes, *i.e.* the quantity $\frac{\text{molecular weight}}{\text{specific gravity}}$.

Kopp (1842) determined the molecular volumes of a number of carbon compounds, and came to the conclusion that in the case of closely related compounds the same difference in composition corresponds with a similar difference in molecular volume, *e.g.*:

		Mol volume.	Difference.
Alcohols,	$CH_3 \cdot OH$	42·2	
			→ 20
	$C_2H_5 \cdot OH$	62·2	
			→ 19·14
	$C_3H_7 \cdot OH$	81·34	
			→ 20·24
	$C_4H_9 \cdot OH$	101·58	
Fatty acids,	$H \cdot CO_2H$	41·4	
			→ 22·3
	$CH_3 \cdot CO_2H$	63·7	
			→ 21·7
	$C_2H_5 \cdot CO_2H$	85·4	
			→ 21·7
	$C_3H_7 \cdot CO_2H$	107·1	

and further, that isomeric liquids have the same molecular volumes, *e.g.* acetic acid 63·7, and methyl formate 63·4; propionic acid 85·4, ethyl formate 85·3, and methyl acetate 84·8. The replacement of an atom of oxygen or an atom of carbon by two atoms of hydrogen does not appear to alter the molecular volume to any considerable extent:

Methyl alcohol, CH_4O....	42·1	Amyl alcohol, $C_5H_{12}O$	124·0
Formic acid, CH_2O_2.......	41·4	Ether, $C_4H_{10}O$.............	106·0
Benzyl alcohol, C_7H_8O...	123·7	Butyric acid, $C_4H_8O_2$.....	107·1

The difference due to a CH_2 group is roughly 22, and since the atomic volume of carbon is twice the atomic volume of hydrogen, it follows that the atomic volume of carbon = 11 and of hydrogen = 5·5. *Kopp* also indicated that the atomic volume of a polyvalent element, *e.g.* oxygen, is not a constant quantity, but varies according to the manner in which the oxygen atom is united to the other atoms in the molecule. Thus in the form of a carbonyl group, $>C:O$, the atomic volume of oxygen is 12·2 (carbonyl oxygen), but in the form of $>C \cdot O \cdot C<$ or $\geqslant C \cdot O \cdot H$ (oxidic oxygen) it has the value 7·8. Similarly, *Schiff* has shown that the carbon atom can have different values according as it is united to another carbon atom by a single, double, or triple bond. Thus each double bond causes an increase of four units in the molecular volume. By means of these atomic volumes it is possible to

calculate the molecular volume of any simple carbon compound, *e.g.* ethyl formate, $H \cdot CO \cdot O \cdot CH_2 \cdot CH_3$,

$$\left.\begin{array}{lcr} 3C & = & 33 \\ 6H & = & 33 \\ 1O: & = & 12{\cdot}2 \\ 1{\cdot}O{\cdot} & = & 7{\cdot}8 \end{array}\right\} = 86{\cdot}0,$$

and the value actually obtained by experiment is 85–86. Although such generalizations as those mentioned are of considerable theoretical importance, the method is not one which has been used to any great extent for determining the constitution of chemical compounds (compare molecular refraction and molecular magnetic rotation). This is partly due to the fact that the specific gravity, and hence the molecular volume, varies with the temperature. At first, *Kopp* made all his determinations at 0°, but obtained better results by taking the specific gravity at the boiling-point of the liquid. It is not necessary actually to make the determination at the boiling-point, but to determine the specific gravity at a lower temperature, and then to correct for the coefficient of expansion as determined by the dilatometer. In reality, the determinations should be made at temperatures when the liquids are all in an exactly comparable condition, viz. at the critical point (compare Zeit. phys. 1890, **6**, 578). More recent determinations of molecular volumes by *T. E. Thorpe* (J. C. S. 1880, 327) indicate that isomeric compounds have not always the same molecular volumes, and that the differences amount to several units per cent., but that elements such as chlorine and bromine in the liquid state have the same atomic volumes as in their organic compounds (compare also *Lossen*, A. 1883, **214**, 138; *Horstmann*, B. 1885, **20**, 766; *Schiff*, A. 1884, **220**, 71; *Zahnder*, A. 1883, **214**, 138; also *Le Bas*, mol. volume of liquid compounds, *Longmans*, 1915.)

D. Molecular Refraction

It has been shown that the molecular refraction, like the molecular volume, is to a large extent an additive property, *i.e.* the molecular refraction is the sum of the atomic refractions of the atoms present in the molecule, but, in addition, that it is to a certain extent constitutive; thus the oxygen atom has distinct atomic refractions according to whether it is in the carbonyl or oxidic state of combination.

The refractive index itself, $n = \frac{\text{sine of angle of incidence}}{\text{sine of angle of refraction}}$, does not lend itself to the study of generalizations, but, according to *Gladstone* and *Dale* (1858), such generalizations are found when the specific refractory power, $\frac{n-1}{d}$ (where d = specific gravity), is employed. This specific refraction varies but little with the temperature; thus with water:

t	0°	10°	20°	90°	100°
Specific refraction..	0·3338	0·3338	0·3336	0·3321	0·3323

and is not largely affected by the presence of other substances. A second formula for the specific refractive power has been introduced by *Lorentz* and *Lorenz*, viz. $\frac{n^2-1}{(n^2+2)d}$; this has the advantage that the value appears to be independent of the physical state of the compound:

		Lorentz-Lorenz		*Gladstone-Dale*	
	t	Gas.	Liquid.	Gas	Liquid.
Water....................	10°	0·2068	0·2062	0·3101	0·3338
Carbon disulphide.....	10°	0·2898	0·2805	0·4347	0·4977
Chloroform.............	10°	0·1796	0·1790	0·2694	0·3000

When the refractive powers of different substances are compared, it is usual to employ the molecular refractive powers rather than the specific refractions. The molecular refraction is the product of the specific refraction into the molecular weight; according to *Gladstone* $\frac{M(n-1)}{d}$, and according to *Lorentz-Lorenz* $\frac{M(n^2-1)}{d(n^2+2)}$.

As the refractive index differs with light of different wave-lengths, it is necessary to determine the value of n for monochromatic light, and to indicate the special light employed; generally determinations are made for the D line in the sodium, or the α line in the hydrogen spectrum, and are carried out in hollow prisms containing the liquid and provided with sides of plate glass.

Landolt examined the molecular refractions of the members of several homologous series, and came to the conclusion that the molecular refraction is an additive quantity, and that similar changes in composition induce similar changes in the molecular refractive power:

Alcohols

	$\frac{M(n-1)}{d}$	Diff.
$CH_3 \cdot OH$	13·17	
		→ 7·53
$C_2H_5 \cdot OH$	20·70	
		→ 7·60
$C_3H_7 \cdot OH$	28·30	
		→ 7·81
$C_4H_9 \cdot OH$	36·11	
		→ 7·27
$C_5H_{11} \cdot OH$	43·38	

Acids

	$\frac{M(n-1)}{d}$	Diff.
$H \cdot CO_2H$	13·91	
		→ 7·20
$CH_3 \cdot CO_2H$	21·11	
		→ 7·46
$C_2H_5 \cdot CO_2H$	28·57	
		→ 7·65
$C_3H_7 \cdot CO_2H$	36·22	
		→ 7·83
$C_4H_9 \cdot CO_2H$	44·05	

and similarly for various groups of esters, the mean value for the CH_2·group being 7·6 units. By methods similar to those described under molecular volumes, values were obtained for the atomic refractive powers of the elements for the a line, *e.g.* C = 5, H = 1·3, O = 3, Cl = 9·79, Br = 15·34, &c. The values thus obtained for the halogens are practically identical with those determined for the elements in the free state. The molecular refraction of any simple carbon compound can be calculated by adding together the atomic refractions of the constituent elements. Thus, for ethyl alcohol, C_2H_6O, the calculated molecular refraction is $2 \times 5 + 6 \times 1{\cdot}3 + 3 = 20{\cdot}8$, and that actually found experimentally is 20·7.

According to *Landolt*, the molecular refraction is purely additive, and thus isomeric compounds should possess identical molecular refractive powers. This is largely true in certain cases, *e.g.* the compounds $C_3H_6O_3$—propionic acid, 28·57; methyl acetate, 29·36; and ethyl formate, 29·18.

In a series of investigations begun in 1878 (A. 1879, **200,** 139; 1880, **203,** 1 and 255) *Brühl* has examined the influence of atomic grouping on the molecular refraction, and has been able to show that the property is not purely additive, but to a certain extent constitutive. Thus a comparison of the experimental and calculated values for unsaturated and the corresponding saturated compounds at once exhibits anomalies:

	$\frac{M(n-1)}{d}$ for a-line. Observed.	Calculated.	Difference.
Allyl alcohol, C_3H_6O	27·88	25·8	2·08
Propyl alcohol, C_3H_8O	28·60	28·4	0·2

Similarly in other unsaturated compounds it is found that a double bond between two carbon atoms usually increases the molecular refraction by about two units (mean value 2·15), and a triple bond by 1·95 unit.

Other polyvalent elements have atomic refractions which

vary with their state of combination; thus oxygen in carbonyl compounds has the value 3·4 in hydroxy-derivatives, and in ethers the value 2·8. The following is a list of some of the more important atomic refractions used by *Gladstone* and by *Brühl*:

	Gladstone.	*Brühl* (*L.-L.* formula).
Carbon in saturated compounds.........	5·0	2·365
Hydrogen....................................	1·3	1·103
Carbonyl oxygen in >C:O..............	3·4	2·328
Ether oxygen in ⋗C·O·C⋖............	2·8	1·655
Hydroxylic oxygen in ⋗C·O·H........	2·8	1·506
Chlorine.......................................	9·9	6·014
Bromine.......................................	15·3	8·863
Iodine..	24·5	13·808
Ethylene bond..............................	2·1	1·836
Acetylene bond.............................	1·95	2·22
Sulphur in C:S..............................	16·0	...
Sulphur in C·S·H..........................	14·1	...
Nitrogen in compounds ⋗C·N⋖......	...	2·76

Brühl has employed the molecular refraction for the investigation of certain tautomeric substances, *e.g.* ethyl acetoacetate. The observed value for the *a* line is 31·89, and the values calculated for the ketonic and enolic formulæ respectively, 31·53 and 32·55:

$CH_3·CO·CH_2·CO·OC_2H_5$			$CH_3·C(OH):CH·CO·OC_2H_5$		
6C	=	14·190	6C	=	14·190
10H	=	11·03	1 ethylene bond	=	1·836
2O (carbonyl)	=	4·656	10H	=	11·03
1O (ether)	=	1·655	1O (carbonyl)	=	2·328
			1O (ether)	=	1·655
		31·531	1O (hydroxyl)	=	1·506
					32·545

The conclusion to be drawn from these numbers is that the ethyl acetoacetate at the ordinary temperature consists mainly of the ketonic form, but probably contains a small amount of the enolic. *Brühl* also tested the purity of numerous compounds prepared by him, by means of molecular refraction and dispersion determinations in place of ordinary combustions. *Perkin* and *Gladstone* have examined the molecular refractive

powers of several di- and triketonic substances. For acetyl acetone at 11°, using the formula $M(n - 1)/d$ for the α line, the value 45·17 was obtained, and this decreased to 44·14 at 99·3°. The ketonic formula requires 42·2, the mono-enolic 43·7, and the di-enolic 45·2. At 11° the diketone undoubtedly consists mainly of the dihydroxylic compound $CH_3 \cdot C(OH)$: $C:C(OH) \cdot CH_3$, and at the higher temperature, probably of a mixture of the mono- and dihydroxylic forms.

Later measurements by *Auwers* (B. 1911, **44,** 3530) for keto-enolic equilibrium mixtures show close agreement with the results obtained by *Meyer* (p. 753), and still later experiments (A. 1918, **415,** 169) show that the examination of specific refractivities and dispersions can be used for differentiating between the keto and enolic forms of simple aldehydes and ketones, but is of no value in the case of β-di-ketones, as the mono-enolic form then contains a conjugate system of double bonds, which produces an abnormal increase in the refraction and still more in the dispersion.

Stereo-isomerides of the type of maleic and fumaric acids have not necessarily the same molecular refraction. Simple ring formation has but little effect on the molecular refraction; in the case of polymethylene compounds it produces an increment of from 0·5 to 0·7, and in discussions bearing on the structure of terpene hydrocarbons weight is attached to the values for molecular refraction, as it is frequently a choice between a bicyclic formula with no double bond or a monocyclic formula with a double bond (B. **33,** 3124; **40,** 1120), the latter producing an increment of 2 units. This method has been used in the case of thujone and sabinene.

A hemicyclic double bond, *i.e.* an olefine linking between a carbon atom in the ring and one in the side chain (cf. terpinolene, p. 621, and β-phellandrene, p. 622), produces a greater exaltation than an olefine linking in the ring, *e.g.* an increase in M_D of 0·4. This generalization is of value in discussions on formulæ of terpene derivatives; for example, it agrees with the hemicyclic linking in camphene.

Conjugation of double bonds produces pronounced exaltation of molecular refractivity, and abnormally high values for M_D can frequently be used as an argument for the presence of such conjugate linkings in the compounds concerned, *e.g.* in the case of α-terpinene (p. 620). The effects of conjugation are not simple, and are dealt with in Chap. L, C.

Auwers and *Eisenlohr* (J. pr. 1910, **82,** 70; Zeit. phys. 1910, **75,** 585; 1912, **79,** 129) have shown that similar relationships hold for specific and molecular dispersivity. The dispersivity is the difference between the refractivities for colours of different wave-lengths, *e.g.*:

$$r_\gamma - r_\alpha = \frac{n^2_\gamma - 1}{(n^2_\gamma + 2)d} - \frac{n^2_\alpha - 1}{(n^2_\alpha + 2)d}$$

$$\text{and} \quad M_\gamma - M_\alpha = \left(\frac{n^2_\gamma - 1}{n^2_\gamma + 2} - \frac{n^2_\alpha - 1}{n^2_\alpha + 2}\right)\frac{m}{d}.$$

For comparative purposes these authors use the values 100 (sp. dispersivity) and find that it varies more markedly than refractivity with constitution.

Auwers and *Schmidt* (B. 1913, **46,** 457) show that normally the values for specific refractivity and dispersive power follow the order acid > chloride > ethyl ester. This also holds for many dibasic acids, and points to the symmetrical structure for succinyl and phthalyl chlorides (pp. 248, 497; also this chapter, section F. For discussion cf. *Lowry*, J. C. S. 1929, 2858).

E. Molecular Magnetic Rotation

This is quite distinct from the ordinary optical activity exhibited by substances with asymmetric molecules, and is common to practically all substances when they are examined by means of a polarimeter in a strong magnetic field. The tube containing the liquid to be examined is placed end on between the two poles of an electro-magnet, these poles being pierced in order that the observer may take readings, and the apparatus is often jacketed in order that the temperature may be kept constant. (For new form of apparatus, see J. C. S. 1906, 608.) When the magnetic field is changed, it is found that the amount of rotation remains the same but changes sign, and in each determination several positive and several negative readings are made. The rotations of all substances are compared with water under the same conditions, and thus the molecular magnetic rotation is $\frac{M a l_1 d_1}{18 a_1 l d}$, where M is the molecular weight of the substance, a its observed rotation using a column of liquid l cm. long, and d the specific gravity of the liquid; 18 is the molecular weight of water, a_1 its observed rotation,

d_1 its density, and l_1 the length of column used. As a rule $l = l_1$ and $d_1 = 1$ (approx.). An examination of different homologous series by *W. H. Perkin, Sen.*, showed that for an increase of CH_2 in the molecule there is usually an increase of 1·023 units in the molecular magnetic rotation. At first, *Perkin* attempted to obtain atomic magnetic rotations for each element in the same manner as already described for atomic volumes and atomic refractions; the values so obtained gave good results with several distinct series, but could not be applied generally. The method of using **series constants** was then adopted. The molecular magnetic rotation r of a compound may be represented as:

$$r = C + n1{\cdot}023.$$

Where C is a constant which varies with different homologous series, n is the number of carbon atoms present.

A few of the constants are:

n-Paraffins	0·513	Higher esters	0·337
iso-Paraffins	0·631	Aldehydes	0·263
n-Alcohols	0·699	Alkyl chlorides	1·988
iso-Alcohols	0·844	Alkyl bromides	3·816
n-Fatty acids	0·391	Alkyl iodides	8·011
Alkyl acetates	0·370		

If in any series it is required to calculate the molecular magnetic rotation of a member, this is readily accomplished by adding $n \times 1{\cdot}023$ to the series constant; thus for *n*-nononic acid we have

$$0{\cdot}391 + 9 \times 1{\cdot}023 = 9{\cdot}598,$$

and the value actually found by experiment is 9·600.

There is usually a definite relationship between the values for an unsaturated compound and its saturated analogue, *e.g.*:

		Diff.			Diff.
Ethyl crotonate	7·589	1·112	Ethyl oleate	21·909	1·112
Ethyl butyrate	6·477		Ethyl stearate	20·797	

With allyl compounds the difference is not so great; thus the difference between allyl alcohol, 4·682, and propyl alcohol, 3·768, is only 0·914, and similarly for other allyl compounds.

These facts have been used as arguments in the determination of the constitution of undecylenic acid (J. C. S. 1886, 205). The difference in molecular magnetic rotation between unde-

cylenic acid, $C_{10}H_{19}\cdot CO_2H$, and undecylic acid, $C_{10}H_{21}\cdot CO_2H$, is 0·897, and similarly for the esters the difference is 0·890. It is argued that this difference approximates to 0·91, the usual difference between an allyl compound and the corresponding saturated derivative, and hence undecylenic acid is presumably an allyl derivative with the formula $CH_2{:}CH[CH_2]_8\cdot CO_2H$.

The molecular magnetic rotation of a complex compound can be calculated by taking as the series constant the mean of the series constants of the various groups of compounds which it represents. Thus ethyl lactate, $CH_3\cdot CH(OH)\cdot CO_2C_2H_5$, possesses the groupings characteristic of an ethyl ester and also of a secondary alcohol; the series constants for these are:

Ethyl ester = 0·337; secondary alcohol = 0·844. Mean = 0·590.

The series constant for ethyl lactate and homologues is thus 0·590, and the molecular magnetic rotation of the lactate

$$5 \times 1{\cdot}023 + 0{\cdot}590 = 5{\cdot}705,$$

which agrees very well with the experimental value, 5·720. The values of their molecular magnetic rotations have been used by *Perkin* in discussions on the constitutions of certain tautomeric compounds, especially those of the keto-enolic type.

In the case of ethyl acetoacetate, the molecular magnetic rotation for the ketonic form may be calculated as follows:

Series constant for alkyl acetate.......	0·370
Series constant for ketone..............	0·375
Mean................................	0·372

Molecular rotation = 6 × 1·023 + 0·372 = 6·510.

For the enolic form—ethyl β-hydroxy-crotonate, $CH_3\cdot C(OH)\cdot CH\cdot CO_2C_2H_5$—the molecular rotation may be calculated by the two following methods:

1.	Molecular rotation of ethyl crotonate..........................	7·589
	OH replacing H as in alcohol....................................	0·194
	Molecular rotation of ethyl hydroxy-crotonate...............	7·783
2.	Molecular rotation for ethyl β-hydroxy-butyrate...........	6·737
	Difference between unsaturated and corresponding saturated compound	1·112
	Molecular rotation for ethyl hydroxy-crotonate............	7·849

The experimental value actually found for ethyl acetoacetate

at the ordinary temperature is 6·501, and this indicates that, at this temperature, the ester consists essentially of the keto-form. Some general conclusions drawn by *Perkin* are:—

(i) That monoketonic compounds and keto-esters, which react as tautomeric substances, as a rule, have the ketonic and not the enolic structure, except when a number of negative groups, such as phenyl and carboxethyl, $\cdot CO_2C_2H_5$, are present. These have an enolizing tendency, as shown in ethyl benzoylacetate, $C_6H_5\cdot CO\cdot CH_2\cdot CO_2C_2H_5$, which, according to *Perkin*, is a mixture of some 75 per cent of the keto- and 25 per cent enolic compound.

(ii) Acetylacetone at 17° consists of a mixture of some 80 per cent of the hydroxy-ketone, $CH_3\cdot CO\cdot CH{:}C(OH)\cdot CH_3$, and some 20 per cent of the dienolic form, $CH_3\cdot C(OH){:}C{:}C(OH)\cdot CH_3$. If alkyl radicals replace the hydrogen atoms of the methylene group of acetylacetone, the tendency to form the enolic form is less marked, whereas the introduction of negative groups, $\cdot CO_2Et$, increases the tendency.

(iii) Rise of temperature favours ketonization.

(For full details, see J. C. S. 1884, 421; 1886, 205, 777; 1887, 362, 808; 1888, 561, 695; 1889, 680; 1891, 981; 1892, 800; 1893, 488; 1894, 402, 815; 1895, 255; 1896, 1025; 1900, 267; 1902, 177, 292.)

F. The Parachor *

This physical constant was introduced by *Sugden* in 1924 for the study of the structure of organic molecules. It is expressed by the equation $P = \frac{M\gamma^{\frac{1}{4}}}{D - d}$ where M = molecular weight and γ, D, and d the surface tension, density of liquid and density of vapour at any temperature, or $P = MC^{\frac{1}{4}}$, where C = Macleod's constant and is equal to $\frac{\gamma}{(D - d)^4}$ (Trans. Far. 1923, 38).

The parachor is an additive and also a constitutive property. Isomeric esters all have the same value, and the positions of the substituents do not affect the parachor of a di-substituted benzene derivative. Cis and trans stereoisomerides usually give the same value for P. In any given homologous series the increment CH_2 corresponds with a rise of 39·0 in P.

* *Sugden*: "The Parachor and Valency", Routledge, 1930.

The closing of a ring has an appreciable effect and is greater with a small than a large ring, and unsaturation as represented by an olefine or acetylene linkage has a most marked effect, whereas conjugation of two olefine linkages produced the same effect as two such bonds further removed in the molecule from one another. The double linking, whether C:C, C:O, C:S, C:N, and N:O, has the same value provided it is non-polar, and similarly the value for C⋮C and C⋮N is the same.

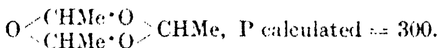
The following atomic and structural parachors have been determined by *Sugden* and others:

C = 4·8, H = 17·1, N = 12·5, P = 37·7, O = 20, S = 48·2, F = 25·7, Cl = 54·3, Br = 68·0, I = 91, triple non-polar bond = 46·6, double non-polar bond = 23·2, 3-membered ring = 16·7, 4-membered ring = 11·6, 5-membered ring = 8·5, and 6-membered ring = 6·1, O_2 in esters = 60·0, not 63·2 (*i.e.* two oxygens plus double bond or 40 + 23·3). For a somewhat different set of values see *Mumford* and *Phillips*, J. C. S. 1929, 2112).

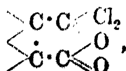
The parachor observed for benzene, viz. 206·2, is almost identical with that calculated for 6C + 6H + 3 olefine bonds + 6-membered ring, *i.e.* 207·1.

The lower value observed in the case of esters may be due to interaction between the two oxygen atoms and a reduction of unsaturation (cf. *Smedley*, J. C. S. 1909, 231).

The parachor value has proved useful in the study of certain structural problems, *e.g.* paraldehyde (p. 136) might have either an open chain structure, $OH{\cdot}CHMe{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2{\cdot}CH{:}O$, P calculated = 317 or the cyclic structure



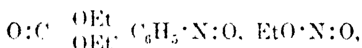
The value actually found, viz. 299, points to the ring formula. In the case of *p*-quinones (Chap. XXV, E) the parachor value points to the ketonic and not the peroxide structure. The symmetrical structure for the chloride of succinic acid, viz. $\frac{O}{Cl}{>}C{\cdot}CH_2{\cdot}CH_2{\cdot}C{<}\frac{O}{Cl}$, agrees best with its parachor value, and of the two phthalyl chlorides the one melting at 15° appears to be the symmetrical and the isomer melting at 88·5 the unsymmetrical,



and thus confirms *Ott* and *Pfeiffer's* view (B. 1922, 413; cf. p. 498).

The values for benzil and similar α-diketones agree with the usual ketonic formulæ rather than with cyclic systems, whereas the colourless isomeric forms sometimes isolated (B. 1922, 1174, 3753; *Irvine*, J. C. S. 1907, 541) are the cyclic or peroxide compounds. Chemically they are far less active.

The study of parachor values has proved most useful in the case of compounds containing double linkages between oxygen and sulphur or oxygen and nitrogen. The parachor values for alkyl carbonates, nitroso-compounds, alkyl nitrites and sulphones as determined experimentally agree perfectly with the values calculated on the assumption that these compounds contain the non-polar double linking between C and O, N and O, S and O, *i.e.* the formulæ,



$$O:C\begin{matrix}OEt\\OEt\end{matrix},\ C_6H_5\cdot N:O,\ EtO\cdot N:O,$$

but with alkyl sulphites, alkyl sulphonates, alkyl sulphates, nitro compounds, azoxy compounds and the N ethers of oximes the observed values for the parachor do not agree with the values calculated from the usual formulæ for these compounds, the observed values always point to a lower degree of unsaturation, *i.e.* fewer non-polar double linkages. These cases are readily explicable if the presence of a semi-polar double bond is assumed.

Polar, non-polar, and semi-polar linkages.—In the ordinary ionizable salts, *e.g.* NaCl, the so-called polar bond or electrovalency is attributed to the loss of an electron from the outer layer of the sodium atom and its passage to the outer layer of the chlorine atom, by this process both ions $\underset{2.8}{\overset{+}{Na}}$ and $\underset{2.8.8}{\overset{-}{Cl}}$ (where the numbers given represent the number of electrons in each layer) become stable as each has an outer envelope of 8 electrons (the stable octet). In this union there is no sharing of electrons, and in the solid state the substance forms a closely packed crystal lattice of ions. These compounds are characterized by having an electric dipole, *i.e.* the electric centre of gravity of the negative charge of the electrons does not coincide with that of the positive nucleus.

Quite different is the type of union which occurs between the atoms of ordinary carbon compounds. Here the common

tions which are not explicable when ordinary dicovalency links are used. (Cf. amine oxides, alkyl sulphites, &c., disulphones, Chap. XLVI E.)

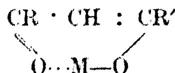
4. On this view a dipole is present in such systems and this will tend to increase the dielectric constant and also association, but to diminish volatility and this is in agreement with what is known of the compounds.

The study of parachor values has proved of value in the following groups:

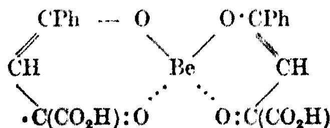
(*a*) Azoimides. Both parachor values (B. 1928, 1529) and molecular refraction and dispersion values (*Philip*, J. C. S. 1908, 918; 1912, 1866) favour *Curtius'* cyclic formula (B. 1890, 3023) rather than the open chain formula II (*Thiele*, B. 1911, 2524).



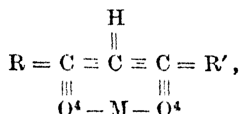
(*b*) Co-ordinate compounds especially the cyclic **chelate** compounds (*Morgan*, J. C. S. 1920, 1457), *e.g.* the metallic derivatives of certain β-diketones or β-ketonic esters in which there is a residual valency between the metal and the O of carbonyl, the ketone $R\cdot CO\cdot CH_2\cdot CO\cdot R'$ reacts in the enolic form to give the metallic derivative $R\cdot CO\cdot CH:C(OM)\cdot R'$ and then the residual valency produces the ring



These are often remarkably stable compounds and the residual or covalency appears to have much the same value as an ordinary valency, especially in stereochemical problems, thus the beryllium derivative of benzoylpyruvic acid exists in optically active forms (*Mills* and *Gotts*, J. C. S. 1926, 3121; cf. *Burgess* and *Lowry*, 1924, 2081; *Mann* and *Pope*, 1926, 2675), indicating that the two ordinary linkages and the two residual valencies around the beryllium atom must be arranged tetrahedrally:



The parachors of several metallic derivatives of β-ketones and β-ketonic esters have been determined (*Sugden*, J. C. S. 1929, 318), and the values are in agreement with those calculated for the electronic formula,



which is symmetrical and represents each atom as perfectly neutral. Here each atom of oxygen has four shared and four unshared electrons and each carbon eight shared electrons. The monovalent metal M shares two electrons with two oxygen atoms, but only one with each. The original diketones should be able to exist in such chelate rings, but determination of parachors prove that there is little or no tendency to the formation of such rings in the case of acetylacetone, propionylacetone, benzoylacetone and boron acetylacetonedifluoride.

For other views on co-ordinate compounds see *Sidgwick*, J. C. S. 1923, 725; B. A. Rep. 1927, 27).

G. Absorption Spectra

Ostwald (Zeit. phys. 1892, **9**, 579) has studied the absorption spectra of groups of closely related coloured compounds, *e.g.* a series of *soluble* metallic permanganates, various salts of fluoresceïn, eosin, and rosolic acid, and has been able to show that, in dilute solutions, the absorption spectrum of a salt is the sum of the spectra of the ions; thus all the permanganates gave practically the same absorption due to the $\bar{Mn_2O_8}$ ion.

Hartley and others have carried out numerous investigations on ultra-violet absorption spectra of carbon compounds, and extremely important relationships have been established. (For references, see B. A. Reports 1900–1903.) *Hartley* photographed the spark spectrum of an alloy of tin, lead, cadmium, and bismuth after it had passed through a solution of the substance under examination. It was found that practically all open-chain and even the closed-chain polymethylene compounds give no distinct selective absorption; they are remarkably transparent to ultra-violet rays. Numerous exceptions, *e.g.* ethyl acetoacetate derivatives,

ketones, and practically all ketonic compounds, whether open chain or cyclic, have since been met with (*Baly* and *Desch* J. C. S. 1904, 1039). In any given series, *e.g.* the alcohols, it is usually found that each increment of CH_2 produces a slight increase in the absorption of the more refrangible rays.

Benzene derivatives, naphthalene, anthracene, phenanthrene, and their derivatives, also pyridine, quinoline, dimethylpyrazin, $N{<}^{CMe\cdot CH}_{CH:CMe}{>}N$, in alcoholic or aqueous solutions, exhibit, in many cases, distinct **absorption bands.** Most of the terpenes, furane, thiophene and pyrrole derivatives, piperidene and reduced benzene derivatives, resemble the aliphatic compounds.

In all cases *Hartley* examined the absorption for solutions of very different concentrations, always increasing the dilution until complete transmission was obtained. He also used layers of the given solutions of different lengths and then plotted the results in the form of curves, putting the oscillation frequencies (reciprocal of wave-lengths) as abscissæ, and equivalent thicknesses of solution as ordinates. Thus with two solutions, one ·01N and the second ·001N, and using layers of each 30, 20, 15, 10, 5 mm. thick, the equivalent thicknesses are 300, 200, 150, 100, 50, 30, 20, 15, 10, and 5, and these numbers are used in the plotting. *Baly* and *Desch* have used the iron arc spectrum and a glass cell with quartz ends for containing the solution, so arranged that the length of the column of liquid can easily be varied. They also plot the oscillation frequencies against the logarithms of the relative thicknesses of liquid. From the absorption curves so plotted it is very much easier to compare the relative persistence of the absorption bands.*

Hartley examined a number of isomeric benzene derivatives, *e.g.* xylenes, cresols, and dihydroxy-benzenes, and found that the oscillation frequency of the extreme rays transmitted follows the order ortho → meta → para, *i.e.* the para-compounds exhibit the greatest absorption. The same generalization does not hold for other groups of compounds, *e.g.* the hydroxy-benzoic acids.

A most important fact is that the introduction of a methyl group for a hydrogen atom affects the absorption spectrum but little; as a rule, it slightly increases the general absorption, but does not alter the general character of the spectrum, *e.g.* benzene and toluene, benzoic acid and methyl benzoate.

* Compare *Henri*, "Études de Photochimie", 1919.

This fact has been largely used by *Hartley* and *Dobbie* in discussions on the constitution of certain tautomeric substances, more especially those of the lactam-lactim type. A study of the general chemical properties of isatin (p. 557) does not render it possible to say whether this compound has the lactam constitution I, or the lactim constitution II:




$$\text{I}\ C_6H_4{<}\begin{smallmatrix}NH\\CO\end{smallmatrix}{>}CO \qquad \text{II}\ C_6H_4{<}\begin{smallmatrix}N\\CO\end{smallmatrix}{>}C{\cdot}OH.$$

Although isatin itself exists in one form only, 5:7-dimethyl-isatin exists both as a lactam melting at 243° and a lactim, red crystals melting at 204°. (B. 1918, **51**, 180, 1270.) Isatin gives rise to the two distinct methyl ethers: (*a*) methyl-isatin, III, a solid melting at 101°, readily hydrolysed, and obtained by the action of methyl iodide on silver isatin; (*b*) pseudo-methyl-isatin, IV, a solid melting at 134°, not readily hydrolysed, and prepared by heating methyl-dibromo-oxindole with water:




$$\text{III}\ C_6H_4{<}\begin{smallmatrix}N\\CO\end{smallmatrix}{>}C{\cdot}OCH_3 \qquad \text{IV}\ C_6H_4{<}\begin{smallmatrix}N(CH_3)\\CO\end{smallmatrix}{>}CO.$$

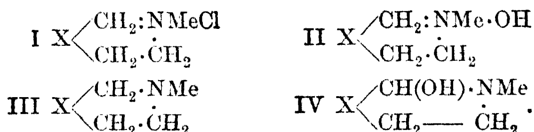
An examination of the absorption curves of the three compounds, isatin, methyl-isatin, and pseudo-methyl-isatin (J. C. S. 1899, 640) shows that the curves for isatin and the pseudo-ether are practically identical, both possessing two bands of similar intensity and differing considerably from that of methyl-isatin, which consists of a single band. There can be no question but that isatin itself has a constitution similar to that of the pseudo-methyl ether; and since the reactions of this prove beyond doubt that it is a nitrogen and not an oxygen ether, isatin must have the lactam constitution represented by formula I. Similarly carbostyril (p. 585), by a comparison of its absorption curve with that of its two methyl ethers, can be shown to possess the lactam constitution I and not the lactim constitution II:




$$\text{I}\ C_6H_4{<}\begin{smallmatrix}CH:CH\\NH{\cdot}CO\end{smallmatrix} \qquad \text{II}\ C_6H_4{<}\begin{smallmatrix}CH:CH\\N{=}C{\cdot}OH\end{smallmatrix};$$

and *o*-oxycarbanil, obtained by fusing *o*-amino-phenol hydrochloride with carbamide, has an absorption spectrum practically identical with that of its N-ethyl ether, and hence has the lactam constitution $C_6H_4{<}\begin{smallmatrix}NH\\O\end{smallmatrix}{>}CO$.

Stereo-isomeric alkaloids give identical absorption spectra (J. C. S. 1900, 498, 509), and the study of absorption spectra has been used to distinguish between the carbinol and ammonium formulæ for hydroxylated alkaloids, *e.g.* cotarnine (p. 602) and hydrastinine. An aqueous solution of cotarnine gives an absorption spectrum similar to that of the hydrochloride in water, whereas a solution of the base in dry ether gives a spectrum similar to that of hydrocotarnine, hence it is concluded that in water the base has the ammonium formula II analogous to the chloride I, whereas in ether it has the carbinol structure IV analogous to hydrocotarnine III, where X = $CH_2O_2:C_6H\cdot OMe$. (Cf. J. C. S. 1911, **99,** 1340; 1914, **105,** 1639.)



Hartley and *Dobbie* (J. C. S. 1900, 498) have also examined the absorption spectra of the three dibenzoyl-succinates obtained by *Knorr*. According to the latter, the α-compound has the enolic constitution I, whereas the two solid β- and γ-compounds are stereo-isomeric ketones with constitution II:



In accord with this view is the fact that the β- and γ-compounds give practically the same spectrum, which differs, however, considerably from that of the α-compound. The transformation of the α- into a mixture of the β- and γ-compounds can readily be followed by examining alcoholic solutions at different intervals of time; at the end of three hours considerable change has taken place, and at the end of three weeks the ketonization is practically complete.

Baly and *Desch* have found that although ethyl acetoacetate in dilute solution, and its two ethyl derivatives $CH_3\cdot CO\cdot CHEt\cdot CO_2Et$ and $CH_3\cdot C(OEt):CH\cdot CO_2Et$, give no selective but only general absorption, the metallic derivatives, *e.g.* ethyl sodio-acetoacetate, have distinct banded absorption spectra, and that even the addition of a small amount of alkali

to ethyl acetoacetate produces a banded spectrum. Acetylacetone itself and its aluminium, beryllium, and thorium derivatives all give banded ultra-violet absorption spectra. Since neither the C- nor the O-ethyl derivative of ethyl acetoacetate produces selective absorption, it would appear that the characteristic band in open-chain compounds cannot be due to either the ketonic or the enolic constitution, and *Baly* and *Desch* drew the conclusion that these absorption bands are only produced by compounds which are in an actual state of change, for example, passing alternately from the ketonic to the enolic form.

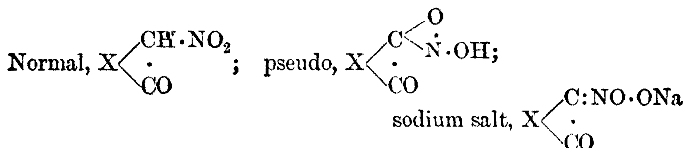
The absorption bands characteristic of simple benzene derivatives may be accounted for in a somewhat similar manner (J. C. S. 1904, 1029; 1905, 1331). In the case of simple benzene derivatives, especially hydrocarbons, seven distinct bands are visible, due to seven distinct valency changes. (Compare also J. C. S. 1906, 514, 983; 1907, 449, 1122; 1908, 1906; 1910, 571, 1337, 1494.)

By means of a fluorspar spectrograph, *Stark* (Abs. 1913, ii, 363, 365, 366) finds evidence of absorption bands in the extreme ultra-violet region given by saturated hydrocarbons such as cyclohexane and camphane. The di- and tetrahydro-benzenes give absorption bands similar to those characteristic of olefine derivatives, whereas benzene gives a totally different spectrum, and this is urged as an argument in favour of some such formula as *Armstrong's* for benzene (p. 360). Conjugation of double bonds produces intensification of the less refrangible bands and a shifting of the bands towards the visible spectrum.

Baly and *Stewart* (ibid. 1906, 489, 502, 618) have examined the absorption curves of various ketones and quinones. Their results with fairly concentrated solutions show that the ketones which show the most persistent absorption bands are those which are most reactive from a chemical point of view, *e.g.* react most readily with sodium hydrogen sulphite or with hydroxylamine. In these cases also, the bands were attributed to actual valency changes (desmotropism) going on in the molecules of the substances. With β-diketones and monoketones the change is between the keto- and enolic forms.

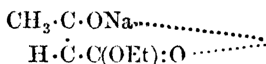
According to *Lowry* and *Desch* (J. C. S. 1909, 807, 1340; 1910, 900), intramolecular change is not always accompanied by selective absorption. The conversion of normal nitrocamphor into

the pseudo-isomeride, a reaction which can be studied quantitatively (p. 763), is not accompanied by any characteristic absorption bands, but such bands make their appearance when an alkali is added, and the addition of an excess of alkali does not produce increased absorption. The absorption cannot be due to tautomeric change, as in the presence of the alkali the nitrocamphor exists as a stable sodium salt. The following formulæ are suggested (where $X = C_8H_{14}$):



Similarly α-bromomethyl camphor gives distinct absorption bands, although isomeric change is not possible. It is thus clear that isomeric change does not always produce selective absorption, and that absorption can occur without any isomeric change.

Hantzsch (B. 1910, **43**, 1549; 1911, **44**, 1771), as the result of spectroscopic investigations of ethyl acetoacetate and its derivatives, draws the conclusion that the specific absorption observed in solutions cannot be due to the enolic modification, nor yet to an oscillation between the ketonic and enolic states, but to an isomeric aci-form in which the residual valencies of the oxygen atoms and of the metal (or hydrogen) of the ONa group are operative, *e.g.*:



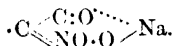
The fact that an increase in the amount of alkali produces an increase in the selective absorption is attributed to the fact that an excess of alkali prevents the hydrolysis of the sodium salt to the enol and sodium hydroxide.

Such formulæ are now explicable on the basis of electronic views, and may be attributed to the formation of a six-membered ring, one atom of which is the divalent metal which shares one electron with each of two oxygen atoms (p. 745). A ring or chelate formula has also been attributed to the enolic form itself (*Sidgwick*, J. C. S. 1925, 907).

The absorption bands of various vapours, *e.g.* benzene, py-

ridine, furane, and thiophene derivatives, have been studied by *Hartley* (Phil. Trans. 1908, A. **208,** 475) and *Purvis* (J. C. S. 1910, 692, 1035, 1546, 1648; 1911, 2318; 1913, 1088, 1636), who show that in the form of vapour these compounds give absorption spectra which are much more complex than those of their solutions.

Nitro Compounds.—The spectroscopic investigations of *Hantzsch* and *Voigt* (B. 1912, **45,** 85; Zeit. phys. 1912, **79,** 592) on aliphatic-nitro compounds indicate the existence of three distinct types of nitro derivatives. (1) True nitro compounds $R\cdot CH_2\cdot NO_2$, which exhibit a very feeble selective absorption. (2) Aci-nitro compounds $R\cdot CH:NO\cdot OH$ (p. 391) with feeble general absorption and are only met with in the case of simple aliphatic-nitro compounds. (3) Conjugate nitro compounds, the usual form in which the metallic salts, derived from nitro compounds with a second negative unsaturated group, such as, CO, NO_2, exist. As the absorption spectra of these compounds is so entirely different from those of the true nitro and aci-nitro derivatives it is argued that they must be differently constituted, and it is suggested that by means of the residual valency of the negative group and of the metallic radical of the NO·ONa group a six-membered ring is formed:



For chromo-isomerism of salts of nitro compounds cf. *Hantzsch,* A. 1911, **384,** 135.

In the case of *p*-nitro-phenol the free phenol and its stable, colourless ethers give absorption spectra resembling those of the conjugate aci-nitro compounds and are represented by formula I. The red metallic salts and the unstable red ethers have far stronger absorption, and are represented as quinonoid compounds exhibiting residual valencies (II).

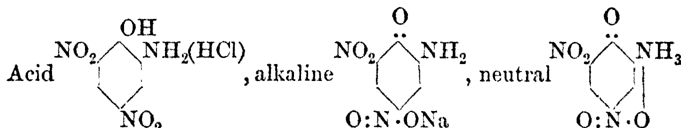




According to *Hewitt,* and others (J. C. S. 1912, **101,** 1770; 1913, **103,** 1626) the reactions of the sodium derivatives of *o*- and *p*-nitro-phenols with ethyl chloro-acetate or sodium methoxide favour the quinonoid rather than the benzenoid structure of the salts of these nitro-phenols, as they react with the reagents mentioned at high temperatures only, whereas

the sodium derivatives of phenol, cresols, halogenated phenols, and even *m*-nitro-phenol react smoothly and readily at 100°. It is also pointed out that only compounds capable of giving rise to quinonoid isomerides give coloured salts with the characteristic ultra-violet absorption.

In the more complicated case of a nitro-amino-phenol it is highly probable that three distinct types exist as indicated by a study of the absorption spectra in acid, neutral, and alkaline solutions; *e.g.* picramic acid (1-amino-4:6-dinitrophenol), *Meldola* and *Hewitt* (ibid. **103,** 876).



For sodium derivatives of nitro-triphenyl-methanes cf. *Hantzsch* and *Hein*, B. 1919, **B52,** 493.

Ethyl Acetoacetate and Keto-Enolic Tautomerism.—The terms desmotropism, tautomerism, and dynamic isomerism have been used by many chemists as more or less synonymous, but the one most commonly used is tautomerism. The example that received the greatest attention for many years was that of ethyl acetoacetate and analogous β-ketonic esters and β-ketones, $R{\cdot}CO{\cdot}CH_2{\cdot}CO{\cdot}R' \rightleftharpoons R{\cdot}C(OH){:}CH{\cdot}CO{\cdot}R'$, which is only an example of the more general case:



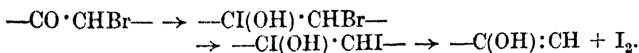
$$A{:}B{\cdot}CH \rightleftharpoons HA{\cdot}B{:}C$$

where A, B and C stand for three atoms of polyvalent elements, for diketones A = oxygen and B and C = carbon. For tautomerism of α and γ ketonic esters, see *Hughes* and *Watson*, J. C. S. 1929, 1945, and α-diketones, *Moureu*, Bull. Soc. 1927, **41,** 1607; C.R. 1928, **186,** 380, 503; 1929, **188,** 504, 1413, 1557). The tautomerism of phenylnitromethane is an example where A = oxygen, B = nitrogen, and C = carbon. In the methyleneazomethine system A and C are carbon, and B nitrogen (J. C. S. 1929, 1199), p-$MeO{\cdot}C_6H_4{\cdot}CH_2{\cdot}N{:}CHPh \rightleftharpoons p$-$MeO{\cdot}C_6H_4{\cdot}CH{:}N{\cdot}CH_2Ph$ where the equilibrium mixture contains 21 per cent of the former and 79 per cent of the latter; and in the equilibrium between an αβ unsaturated acid and its βγ isomeride all three, A, B and C, are carbon atoms.

The conclusion that ethyl acetoacetate is an equilibrium mixture of the ketonic and enolic modifications—a conclusion based mainly on the study of physical properties (cf. p. 734)—has been confirmed quite recently by other methods.

1. *Knorr* (B. 1911, **44,** 1138) has shown that, by cooling to $-78°$ a solution of the ordinary ester in alcohol and ether in an apparatus specially designed to exclude moisture and to maintain a high vacuum, the ketonic form separates as well-defined needles or prisms, m.-pt. $-39°$ and b.pt. 39°–40°/2 mm. It does not give a coloration with ferric chloride, and does not react with bromine solution. Even at the ordinary temperature it takes several weeks before the equilibrium mixture is again formed. The practically pure enol is obtained by suspending the sodium derivative in light petroleum cooled to $-78°$ in a special apparatus, and passing in hydrogen chloride just insufficient for complete decomposition. The solution when filtered and evaporated at $-78°$ yields the enolic ester as a colourless oil, which gives an intense coloration with ferric chloride. At the ordinary temperature it requires ten to fourteen days to again form the equilibrium mixture, but at 100° the change is completed in one minute. By comparing the refractive index of the ordinary ester with the values for mixtures of known concentration, it has been calculated that the equilibrium mixture contains 7 per cent of the enol (cf. *Meyer* and *Willson*, B. 1914, **47,** 837).

2. By means of experiments made with compounds which exist in stable keto and enolic forms, *K. H. Meyer* (A. **380,** 212; B. **44,** 2718) shows that the unsaturated hydroxylic modification reacts instantaneously with an alcoholic solution of bromine, yielding an unstable dibromide, which immediately gives off hydrogen bromide and forms the bromo-ketone. The best method for estimating the amount of enol is to add an excess of the alcoholic bromine solution, to remove the excess by means of β-naphthol, and then to determine the amount of bromo-ketone by adding potassium iodide solution, and titrating the liberated iodine by means of standard thiosulphate:



$$\text{—CO·CHBr—} \rightarrow \text{—CI(OH)·CHBr—} \rightarrow \text{—CI(OH)·CHI—} \rightarrow \text{—C(OH):CH} + I_2.$$

In this way it has been shown that the ordinary ethyl acetoacetate contains about 7 per cent of the enol, and the same

results are obtained when freshly prepared solutions in various solvents are examined; but such solutions, when kept, undergo change, *e.g.* a hexane solution when kept for forty-eight hours at 18° contains nearly equal amounts of keto and enolic modifications. A rise in temperature also tends to favour the formation of the ketonic form. In a similar manner acetylacetone has been shown to contain 80 per cent of enol.

Further investigations (B. 1912, **45,** 2843) have shown that the solid crystalline forms are not equilibrium mixtures, but consist of the one modification only and that the mixture is formed on solution. In alcoholic solution acetaldehyde, acetone, pyruvic acid, and acetophenone exist almost entirely in the ketonic form, even when sodium alcoholate is present. In compounds containing methylene attached to two COX groups where X = H, Me, Ph, OH, OMe, OEt, NHPh, CO_2Me, and CO_2Et, the following is the relative order of the enolising effect of the radical X: OMe, OEt, OH, NHPh, Me, Ph, CO_2Et, CO_2Me. Ethyl malonate exists almost entirely in the keto form and the sodium derivative has the enolic structure, $CO_2Et{\cdot}CH{:}C(ONa){\cdot}OEt$, but when acidified the enolic modification changes rapidly to the keto form.

The solvent has a marked effect upon the equilibrium, thus the percentage of enolic form in solutions of methyl benzoylacetate, $C_6H_5{\cdot}CO{\cdot}CH_2{\cdot}CO_2Me$, is as follows: water, 0·8, methyl alcohol, 13·4, chloroform, 15·4, hexane, 69, and the same solvent has much the same effect on different tautomeric substances. The reaction with bromine appears to be unaffected by light, and in this respect differs from ordinary bromine substitutions and from the addition of bromine to unsaturated $\alpha\beta$ acids (p. 836).

Meyer's bromine method may also be used for ascertaining the amount of aci-form present in a nitro compound. In the case of phenyldinitro-methane, as the aci compound is more soluble in water or alcohol than the true nitro compound, these solvents tend to bring about the change: aci → true nitro (B. 1914, **47,** 2374; A. 1913, **396,** 133, **398,** 49). The bromine method indicates that the varying crystalline forms of methyl (or ethyl) formylphenylacetate all have enolic structures, $OH{\cdot}CH{:}CPh{\cdot}CO_2Me(Et)$ (*W. Wislicenus*, A. 1916, **413,** 216; *Dieckmann*, B. 1917, **50,** 1375).

Kaufmann and *Richter* (B. 1925, 216) show that the capacity to add bromine is not a characteristic property of all

enols as it may be suppressed by steric influences or by the presence of negative groups.

3. *Knorr* and *Schubert* (B. 1911, **44**, 2772) use a colorimetric method for estimating enols in all allelotropic mixtures, a method which is based on the reaction between the enol and ferric chloride,



$$RH + FeCl_3 = FeRCl_2 + HCl,$$

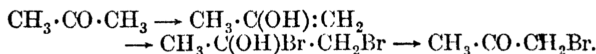
where R is the enolic residue. The comparison is made with standard solutions prepared by mixing solutions of the pure enol with one of sublimed ferric chloride in molecular proportions. For exceptions see B. 1925, 216, and 1560.

4. **Ozone** (*Scheiber* and *Herold*, A. 1914, **405**, 296). This reagent has no enolising action on the keto-enolic equilibrium mixture and immediately transforms the enol into an ozonide (p. 694), but does not attack the keto form. By examining and estimating the products formed by the action of water on the ozonide the structure of the enolic form and a rough estimate of the amount present can be ascertained. In most cases the results confirm those arrived at by other methods. In the case of benzoylacetone where isomeric enolic forms are possible, the results show that in chloroform solution it exists mainly as $C_6H_5 \cdot C(OH):CH \cdot CO \cdot CH_3$, as the products formed from the ozonide are benzoic acid and methyl-glyoxal $CHO \cdot CO \cdot CH_3$. The results with oxalacetone, $CH_3 \cdot CO \cdot CH_2 \cdot CO \cdot CO_2Et$, indicate the presence of two mono-enolic and one di-enolic form viz., $CH_3 \cdot CO \cdot CH:C(OH)$, CO_2Et, $CH_3 \cdot C(OH):CH \cdot CO \cdot CO_2Et$ and $CH_3 \cdot C(OH):C:C(OH) \cdot CO_2Et$ (cf. also B. 1914, **47**, 2704).

In all cases where the composition of the equilibrium mixture is determined by the action of chemical reagents and not from a study of physical constants, the possibility of the enolising action of the reagent employed must be borne in mind. It is claimed that substances such as bromine and ozone have no enolising effects, and hence the conclusions derived from the reactions should agree with those based on physical constants. On the other hand, it is well known that alkalies have a considerable enolising effect,* and the sodium

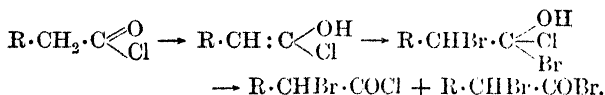
* The enolising effect of traces of alkali is well shown in the case of dibenzoylacetylmethane. The m.-pt. of the compound when determined in Jena glass tubes is 149–150°, but in soft glass tubes falls to 107–110° owing to traces of alkali in the soft glass producing partial enolisation. (*Dieckmann*, B. 1916, **49**, 2203.)

derivatives of esters which can react as tautomerides are usually represented as derived from the enolic forms. Enolisation of simple aldehydes and ketones can also take place in the presence of certain reagents. Thus the sodium derivatives of ketones or aldehydes (p. 143) are represented as enolic compounds (*Freer*). *Grignard* reagents favour enolisation of β-ketonic esters (*Grignard*, C. R. 1902, **134**, 849; *Hepworth*, J. C. S. 1919, 1205), and can produce enolisation in ordinary aldehydes and ketones (*Bhagvat* and *Sudborough*, J. I. I. S. 1919, 187). According to *Lapworth* (J. C. S., 1904, **85**, 30), the bromination of a ketone is preceded by the enolisation of the ketone, the enol then forms an additive compound with bromine, and hydrogen bromide is finally eliminated,



Dawson (ibid. 1909, **95**, 1860; 1912, **101**, 1503; 1914, **105**, 387, 532) claims that similar reactions take place during the bromination of aldehydes and the presence of mineral acids accelerates the bromination by increasing the rate of enolisation.

Aschan (B. 1912, **45**, 1913; cf. *Smith* and *Lewcock*, ibid. 2358; *Ward*, J. C. S. 1922, 1161) concludes that the same generalizations hold good for the bromination of acids by the *Hell - Volhard - Zelinsky* method (p. 175), as the result of brominating an acid chloride is a mixture of the acid chloride and acid bromide of the α-bromo-acid,

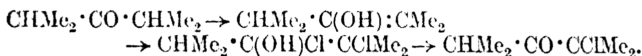


The argument, however, is not conclusive, as similar results might be produced by direct substitution. The conversion of acetyl chloride into acetyl bromide by means of hydrogen bromide and the converse change are also probably due to the intermediate formation of an additive compound between the enolic form and the halogen hydride.

Meyer (ibid. 2864) has been able to show that the reaction between bromine and malonic acid is uni- and not bi-molecular, as it should be if the reaction is one of direct substitution. The fact that the reaction is uni-molecular, and independent

of the concentration of the bromine, is in complete harmony with the view that the reaction actually measured is the enolisation $CO_2H \cdot CH_2 \cdot COOH \rightarrow CO_2H \cdot CH:C(OH)_2$, and that the subsequent reactions are extremely rapid compared with this.

Favorski (Abs. 1913, i, 12) shows that PCl_5 and PBr_5 produce enolisation in the case of certain ketones. The normal reaction with PCl_5 consists in replacing O by Cl_2, $R \cdot CO \cdot R' \rightarrow R \cdot CCl_2 \cdot R'$. In the case of di-isopropyl ketone, however, the chief product is isopropyl-α-chloroisopropyl ketone, $CHMe_2 \cdot CO \cdot CClMe_2$, probably formed by the following series of reactions:



$$CHMe_2 \cdot CO \cdot CHMe_2 \rightarrow CHMe_2 \cdot C(OH):CMe_2 \rightarrow CHMe_2 \cdot C(OH)Cl \cdot CClMe_2 \rightarrow CHMe_2 \cdot CO \cdot CClMe_2.$$

It is possible that the bromination and chlorination of *all* aldehydes, ketones and acids, is not preceded by enolisation: *Leuch's* observation (B. 1913, **46**, 2435) that in the bromination of *d*-β-carboxybenzyl-α-hydrindone,



$$C_6H_4 <\begin{matrix} CH_2 \\ CO- \end{matrix}> CH \cdot CH_2 \cdot C_6H_4 \cdot CO_2H,$$

although the monobromo derivative, obtained by replacing the H atom of the **CH** group by bromine, is mainly the racemic compound, yet possesses a rotation denoting the presence of 10 per cent of the *d*-bromo derivate, *may* indicate that the whole of the bromine compound has not been formed through the intermediary of the enolic compound, as the formation of this compound would destroy the asymmetry of the molecule, and hence the optical activity. *Lapworth* (P. 1913, **29**, 289) concludes that the bromination may have been entirely by means of the enolic compound, and that the small amount of *d*-bromo-acid is due to an asymmetric synthesis from the enol in the presence of the unchanged optically active keto form.

It has been suggested that in certain cases of keto enolic tautomerism, the hydrogen required to produce the hydroxy group does not come from CH or CH_2 between two CO groups. Thus *Brühl* represented ethyl diacetyl-malonate by the enolic formula I, in which the hydrogen



$$\text{I} \quad \begin{matrix} CH_2:C(OH) \\ CH_2:C(OH) \end{matrix} > C(CO_2Et)_2 \qquad \text{II} \quad \begin{matrix} CH_2:C(OH) \text{——} \\ CH_3 \cdot CH:C(OH) \end{matrix} > C(CO_2Et)_2$$

is derived from a terminal CH_3 group. This has been shown by *Auwers* and *Auffenberg* (B. 1917, **50**, 929) to be incorrect. The monoacetyl derivative has the normal enolic structure $CH_3 \cdot C(OH):C(CO_2Et)_2$, and when further acetylated gives the O-acetyl derivative $CH_3 \cdot C(OAc):C(CO_2Et)_2$, which is identical with *Brühl's* compound. The proof of the structure of the compounds is largely based on the fact that two different products are formed (*a*) by first introducing acetyl and then propionyl, (*b*) by first introducing propyl and then acetyl, whereas, according to *Brühl's* scheme the two products should be identical, viz. II.

Another type of tautomerism which has been studied is what is termed **intra-annular** tautomerism. An example studied in detail is the bicyclic system I, where X = CO_2H,



From its method of formation the acid undoubtedly has the structure I, but in the presence of a suitable reagent for unsaturated compounds behaves as II (*Farmer*, *Ingold*, and *Thorpe*, J. C. S. 1922, 128). By careful oxidation with ferricyanide the chief product is caronic acid, 1:1-dimethylcyclopropane-2:3-dicarboxylic acid, and with cold alkaline permanganate $\alpha\alpha$-dihydroxy-$\beta\beta$-dimethylglutaric acid. Another example is the equilibrium,



(J. C. S. 1922, 3303.)

The equilibrium



spoken of as **ring chain** tautomerism has been investigated (J. C. S. 1923, 113, 1683; 1924, 1830; 1925, 1687) in potassium hydroxide and with different groups R and R′. When these are H or Me, the keto form is favoured, but when Et or Pr an equilibrium of keto and enolic form is obtained and with RR′ represented by a spiro cylcopentane group the hydroxy acid alone is formed.

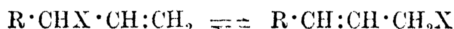
Phthalonic acid, $o\text{-}C_6H_4<\begin{matrix}CO\cdot CO_2H\\ CO_2H\end{matrix}$, exhibits ring-chain tautomerism (Annales, 1927, [X], **7**, 275; **8**, 120) as does also the 4:5-dimethoxy derivative (J. C. S. 1923, 2094). It yields a normal anhydride $C_6H_4<\begin{matrix}CO\cdot CO\\ \vert \\ CO\cdot O\end{matrix}$, but can also give derivatives of the type $C_6H_4<\begin{matrix}C(OR)\cdot CO_2H\\ >O\\ CO\end{matrix}$ and two distinct methyl esters $C_6H_4<\begin{matrix}CO\cdot CO_2Me\\ CO_2Me\end{matrix}$ and $C_6H_4<\begin{matrix}C(OMe)\cdot CO_2Me\\ >O\\ CO\end{matrix}$.

Another example is met with in phorone $CO<\begin{matrix}CH:CMe_2\\ CH:CMe_2\end{matrix}$, the bromo hydroxy derivative of which is undoubtedly cyclic $CO<\begin{matrix}C(OH)\cdot CMe_2\\ \vert \qquad \vert\\ CBr\ \cdot\ CMe_2\end{matrix}$ (J. C. S. 1928, 1868, 2360).

Attempts to represent the phenomena of tautomerism of different types by means of electronic conceptions of the atom structure and to correlate these phenomena with those of intramolecular rearrangement, *e.g.* pinacoline, Wagner-Meerwein, &c., have been made and met with considerable success, but the results do not admit at present of simple representation (see Rep. 1927, 106; 1928, 118; 1929, 116). The term **prototropy** has been suggested for all cases of mobile hydrogen, or mobile proton tautomerism. The proton separates from the system leaving a complex anion which can undergo electron changes. The mobility of the system is largely a measure of the tendency to ionization of the hydrogen ion and the stability of the anion. In symmetrical triad systems (p. 752) mobility depends on the terminal atoms of the system and the character of the central atom has little effect, thus the systems $\cdot NH\cdot CR:N\cdot$ and $\cdot NH\cdot N:N\cdot$ are very similar, and both highly mobile. Mobility in a system can be induced externally by the addition of a catalyst which attracts the mobile proton, *i.e.* by the addition of anions of high co-ordinating power, *i.e.* entities with strong proton affinity. Internal promotion can be effected by constitutional factors, *e.g.* electron affinity of the groups present. In the case of the alkali alkyloxides, *i.e.* of the anions $R\bar{O}$ as catalysts for prototropic change, the order of diminishing efficiency is isopropyl, propyl, ethyl,

methyl, hydrogen. (Cf. *Ingold* and *Schoppee*, J. C. S. 1929, 1199).

Anionotropy is applied to the change involving the wandering of a group or atom which can form a stable anion, *e.g.* ·Cl, ·Br, ·OH, ·OMe, ·O·CO·CH_3, &c.; cf. J. C. S. 1928, 904, 1650; 1929, 455; 1930, 248. *Burton* has examined the system



$$R\cdot CHX\cdot CH{:}CH_2 \rightleftharpoons R\cdot CH{:}CH\cdot CH_2X$$

where R represents a hydrocarbon radical and X a potential anion ·Br, ·O·CO·CH_3, ·O·CO·CCl_3, ·O·CO·C_6H_4·NO_2, and finds that the change depends (*a*) on the nature of R, *e.g.* phenyl is more active than alkyl, (*b*) on the ionic stability of X according to the order Br > O·CO·CCl_3 > O·CO·C_6H_4·NO_2 (*p*) > OH, (*c*) some property of the solvent closely allied to its dielectric constant.

An interesting case, where both prototropy and anionotropy come into play, is that of trialkyl γ-chloroallyl ammonium salts $CH_2Cl\cdot CH{:}CH\cdot NR_3X$ (J. C. S. 1929, 8).

The term **valency tautomerism** is used to connote tautomerism within a neutral molecule and not in an ion.

H. **Anomalous Electric Absorption.**—*P. Drude* (B. 1897, **30**, 941) has found that numerous organic compounds containing hydroxyl groups are capable of absorbing electric waves of high frequency (about 400 million per second), although they are not good conductors; whereas ordinary non-conductors show no such absorption. The phenomenon is termed by *Drude* "**anomalous electric absorption**", and, with the exception of water, all liquid hydroxyl derivatives display this anomalous absorption. The presence of hydroxyl groups cannot always be inferred from the exhibition of anomalous absorption, as a few compounds which contain no hydroxyl groups possess the property to a slight extent.

Drude himself applied the method to the examination of certain keto-enolic tautomeric substances. Ethyl acetoacetate itself absorbs but slightly, and is thus presumably mainly the keto-form.

Ethyl benzoylacetate and ethyl oxalacetate absorb strongly, and should thus contain considerable percentages of the enols.

I. Optical Activity

Attention has already been drawn to the fact that compounds, the molecules of which are dissymmetric (cf. p. 701) are, when in the liquid or dissolved state, optically active, *i.e.* able to rotate the plane of polarization (p. 160) either to the right (dextro-rotatory) or to the left (lævo-rotatory). The specific rotatory power $[\alpha]$ of a liquid is obtained by dividing the observed rotation by the length of the column of liquid used and by the specific gravity of the liquid $[\alpha] = \frac{\alpha}{l \times d}$, and the molecular rotation is the product of the specific rotatory power into the molecular weight (M).

For a solution:

$$[\alpha] = \frac{100\alpha}{l \times c} = \frac{100\alpha}{l \times p \times d} = \frac{100\alpha \times v}{l \times g},$$

where c = concentration or number of grams of the active compound in 100 c.c. of solution, d = specific gravity of the solution, p = per cent of active substance in the solution, and g = number of grams of active substance in v c.c. of solution. The specific rotatory power of a solution may often be increased enormously by the introduction of an inorganic salt; some of the most effective are boric acid and alkali molybdates and tungstates. As a rule, the nature of the monochromatic light, *e.g.* sodium light, is indicated, also the temperature and the nature of the solvent, *e.g.* $[\alpha]_D^{15°}$, where D indicates that the number refers to sodium light and that the determination was made at 15°. Various attempts have been made to deduce general conclusions bearing upon the amount of rotation and the constitution of the compound. *Guye* (C. R. **110,** 714) has attempted to connect the degree of asymmetry of the molecule of a compound C a, b, c, d with the masses of the four radicals present and the distance of the centre of gravity of the molecules from the centre of the tetrahedron (C. R. 1896, 1309; 1898, **181,** 307). The researches of *P. F. Frankland* and others (J. C. S. 1899, 337, 347, 493, &c.) have shown that *Guye's* conclusions are not of general application.

Patterson (for summary see Trans. F. Soc. 1914, **10,** 111, also J. C. S. 1914, **105,** 2322; 1916, **109,** 1139, 1176, 1204) has made a careful investigation of the influence of solvent,

temperature, &c., on the rotary powers of various substances. He finds that *dilute* solutions of ethyl tartrate in water, or in methyl, ethyl, or propyl alcohol, possess a higher specific rotation than the pure ester itself, that the specific rotation increases with dilution until a concentration of 10 grams in 100 grams of solvent is reached, and then the rotation remains practically constant. The highest values are always obtained with aqueous solutions, and the other solutions follow in the order—methyl, ethyl, *n*-propyl, isobutyl, and sec-octyl alcohol.

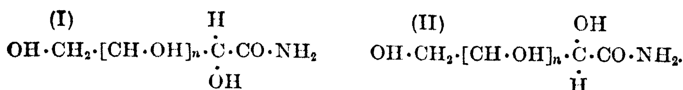
The effect of increase of temperature upon corresponding solutions varies somewhat. In water the coefficient is negative for dilute solutions, but in the various alcoholic solutions it is positive, as it is also for the pure ester.

According to *Patterson* the change in specific rotation with solvent or temperature is not to be attributed to association but rather to the internal pressure of the solvents. (For a summary of work on optical activity see *Walden*, B. 1905, **38,** 345–409, *Frankland*, J. C. S. 1912, **101,** 658, and for effect of solvent, *Patterson*, ibid. 1916, **109,** 1139).

The different effects which two isomerides have on the rotation of ethyl tartrate, *e.g.* the syn- and anti-forms of an oxime, the true and aci- forms of ω-nitrotoluene, and the keto and enolic forms of phenyl-formyl-acetic ester can be used for determining the velocity at which the one isomer becomes transformed into the other. (*Patterson* and others, J. C. S., 1907, 504; 1908, 1048; 1912, 27, 2100; 1929, 1895.)

Pickard and *Kenyon* have determined the rotations of the different members of the series of carbinols, R·CH(OH)Me, R·CH(OH)Et, and R·CH(OH)·$CHMe_2$, and the esters, R·CO·OCHR′CH_3 (J. C. S. 1911, 45; 1912, 620, 1428; 1913, 1923; 1914, 830, 1115, 2226, 2262), and draw the conclusion that there is no simple numerical relationship between the values for the members of any homologous series. For effect of substituents in *o*-benzoic esters, cf. J. C. S. 1929, 2274, 2516.

In the case of amides of the gluconic acid series, *Hudson* (J. A. C. S. 1918, **40,** 813) finds that the spatial arrangements of the α-carbon atom are the deciding factor in determining the nature of the rotation. In all cases compounds in which the group can be represented as in I are *d*- and as in II *l*-rotatory.



Numerous experiments have also been made on rotatory dispersion, and it has been found that *Biot's* generalization that the rotation varies inversely with the wave length is by no means true, and cases of anomalous dispersion are common (*Patterson*, J. C. S. 1916, **109**, 1139, 1176; *Tschugaeff*, Trans. F. Soc. 1914, **10**, 28; *Lowry* and *Austin*, Bakerian Lecture, T. R. S. 1921).

The polarimetric method has been used by *Lowry* (J. C. S. 1899, **75**, 211) for a quantitative study of the tautomerism or dynamic isomerism of the nitro- and bromo-nitro-camphors.

Each of these compounds appears to exist in two distinct forms, one of which contains the nitro-group, $CH\cdot N\begin{smallmatrix}O\\O\end{smallmatrix}$, and the other the isonitro-group C:NO·OH. Ordinary crystalline nitro-camphor, melting at 102°, is regarded as consisting of the normal form, its homogeneity being vouched for by the constancy of its initial specific rotatory power ($[\alpha]_D = -124°$ in 5-per-cent benzene solution), and by its well-defined crystalline form. When dissolved the nitro-compound at once begins to change into the pseudo form, and this change is accompanied by an alteration in the rotatory power; with the 5-per-cent benzene solution the specific rotatory power has fallen to −104° at the end of four days, and then remains stationary. This solution represents a mixture of the normal and pseudo-compounds in dynamic equilibrium, and assuming that the pseudo-compound, which so far has not been obtained in a pure form, has a specific rotatory power +180° in benzene solution, then the solution with a rotation of −104°, contains some 93 per cent of the normal and 7 per cent of the pseudo form.

The velocity of the transformation, normal → pseudo, is increased by rise of temperature, by increase in concentration, and by the addition of traces of alkalis.

The polarimetric method has also been used for measuring the velocity change of *l*-menthyl *d*-phenyl-acetoacetate, $CH_3\cdot CO\cdot CHPh\cdot CO_2\cdot C_{10}H_{19}$, into the enolic form $CH_3\cdot C(OH):CPh\cdot CO_2\cdot C_{10}H_{19}$ (A. 1913, **398**, 372).

Mutarotation.—The change in rotation of an optically active solution is usually known as **mutarotation** (p. 321), and

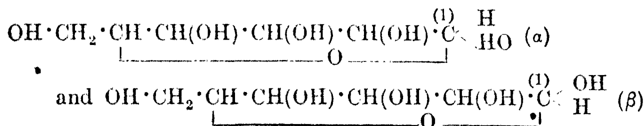
is a property exhibited by various optically active compounds, especially sugars, *e.g.* glucose, galactose, xylose, milk-sugar, and maltose, and certain hydroxy-acids and their lactones, *e.g.* anhydrous lactic acid. In all these cases the rotation changes when the solution is kept; with glucose, for example, the value decreases to half, with milk-sugar the values are as 1·6:1, with galactose 1·46:1, and with xylose 4·67:1. The rotatory powers of maltose and lactic acid solutions increase when kept.

All acids and alkalis appear to facilitate the conversion, and in the order of their degree of ionization. Common salt, alcohol, and various organic compounds, on the other hand, tend to retard the transformation.

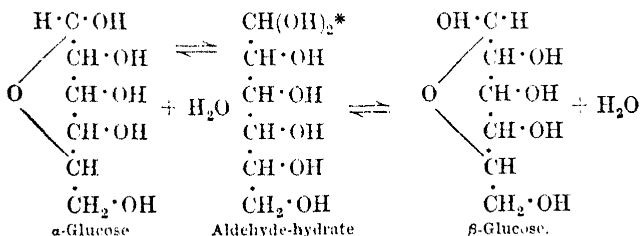
Various theories have been brought forward in order to account for the phenomenon. The first of these assumed the presence of complex molecules, *e.g.* $(C_6H_{12}O_6)_x$, in the freshly-prepared solution, and the gradual decomposition of these into the simpler molecules, $C_6H_{12}O_6$, thus producing a lowering of the rotatory power. The assumption of the presence of complex molecules was rendered untenable as soon as it was shown that the molecular weight, as determined by the cryoscopic method, is the same in the freshly-prepared and the old solution. The second explanation was that, after solution, water is either withdrawn from or added on to the original molecular aggregates. The latest theory is that the different rotations are due to different isomeric substances present in the two solutions, and that a gradual change in rotation accompanies the conversion of the one isomeride into the other.

Tanret (1895) claimed to have isolated three distinct modifications of *d*-glucose, which had the respective specific rotatory powers $\alpha = +105°$, $\beta = +52·5$, and $\gamma = +22·5$. More recent work (*E. F. Armstrong*, J. C. S. 1903, 1305; 1904, 1043) indicates that in the case of *d*-glucose only two distinct isomerides actually exist in solution, viz. the α and γ, and that the so-called β-modification is merely a mixture of the α and γ in chemical equilibrium. The α- and γ-modifications are represented as stereo-isomeric, and correspond in structure with the α- and β-methyl-glucosides (pp. 322, 646), since these glucosides, when hydrolysed with enzymes, have rotatory powers of the order of those of the α- and γ-glucoses, and the addition of an alkali to the products of hydrolysis produces

the same change as with the α- and γ-sugars. They are therefore now termed α- and β-glucoses, and may be represented by the following configurations, the only difference between the two being the spatial arrangements of the radicals around the terminal C atom numbered (1):



(Compare also *Behrend* and *Roth*, A. 1904, **331**, 359, and *Lowry*, J. C. S. 1904, 1551). Both α and β compounds can be isolated in a state of purity by crystallizing *d*-glucose from acetic acid, in the one case at the ordinary temperature and in the other hot (*Hudson* and *Dale*, J. A. C. S. 1917, **39**, 320). The α compound has α_D + 111·2°, and the β + 17·5 (ibid. 1919, **41**, 559). *Lowry* concludes that in an ordinary solution of glucose, in addition to the α- and β-modifications, small amounts of the aldehyde or aldehyde-hydrate are also present. This accounts for the aldehydic properties of glucose solutions, and also affords an explanation of the conversion of the α- into the β-glucose:

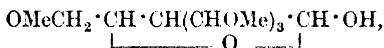


α-Glucose Aldehyde-hydrate β-Glucose.

E. F. Armstrong (J. C. S. 1903, 1305) suggests that the mutarotation proceeds through the addition of water to the oxygen atom of the ring, *e.g.* $>O<^{OH}_{H}$, and *Irvine* and *Steele* (1915, 1230) arrive at the same conclusion from a study of the electrical conductivity of aqueous solutions of tetra-

* A definite open chain glucose derivative with the reducing group exists in pentacetylglucose with zero rotation.

methyl-α-glucose. According to *Boeseken* (B. 1913, 2612; Rec. trav. 1915, **34,** 96, 272), a marked exaltation in the electrical conductivity of boric acid is produced by the addition of a carbon compound containing hydroxyl groups attached to adjacent atoms. When tetramethyl-α-glucose,



with only one OH group, is dissolved in dilute boric acid solution the conductivity of the system gradually rises to a maximum which persists when mutarotation is complete. This points to the addition of OH (*i.e.* water) to the ring O atom, adjacent to the ·CH·OH group, and thus the equilibrium is not between the simple α and β sugars, but between the corresponding oxonium hydrates. By the aid of models it can be seen that by the elimination of water from the oxonium hydrate, and by the shifting of an atom of H from O to C, the conversion of the α sugar into the β is possible. It is probable that the mutarotation of α-glucose itself is therefore due to the formation of oxonium hydrates. Mutarotation can also occur in non-aqueous solvents, *e.g.* acetone or formamide (*Mackenzie* and *Ghosh*, P. R. S. Edin. 1914, **35,** 22), and it is probable that in these cases also the enolised solvent forms oxonium compounds with the ring O atom of the sugar. (For *resumé*, see *Lowry*, B. A. Rep. 1904, 193; *Irvine* and *Steele*, J. C. S. 1915, **107,** 1230.)

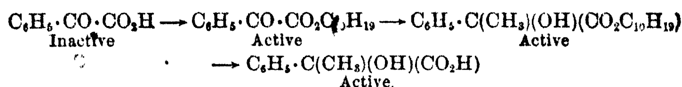
Asymmetric Synthesis.—It has already been stated that the product formed by the synthesis of a compound containing an asymmetric carbon atom from symmetrical compounds is always a mixture or compound of the *d*- and *l*-modifications in equal amounts, and a single active modification can only be obtained by the resolution of this racemic compound or mixture. Numerous attempts have been made to carry out an asymmetric synthesis, *i.e.* according to *Marckwald* (B. 1904, **37,** 1368), to obtain artificially an optically active compound from a symmetrical substance by the employment of an active product but without the use of an analytical process (such, for example, as those involved in the usual separation of racemic mixtures). A synthesis suggested by *E. Fischer* was as follows:—By the cyanhydrin reaction mentioned on p. 315 it is possible to transform an optically active monose containing C_n into a mixture of two active sugars containing C_{n+1}. The amounts of the two

active compounds vary considerably in different cases, and with *d*-mannose only one *d*-mannoheptose can be isolated. Similarly the *d*-mannoheptose yields only one mannooctose, and this only one nonose. If it were possible by some method to decompose this *d*-manno-nonose so as to regenerate *d*-mannose then the other product would be an active glyceric aldehyde:


Mannononose, $CHO \cdot CH(OH) \cdot CH(OH)—CH(OH) \cdot [CH \cdot OH]_4 \cdot CH_2OH$


→ glyceric aldehyde, $CHO \cdot CH(OH) \cdot CH_2 \cdot OH$ and
$CHO \cdot [CH \cdot OH]_4 \cdot CH_2 \cdot OH$.

Cohen and *Whiteley* (J. C. S. 1901, 1305), starting with cinnamic acid, prepared active amyl and menthyl esters, to which they added bromine and then attempted to obtain an active cinnamic acid dibromide, $C_6H_5 \cdot CHBr \cdot CHBr \cdot CO_2H$, by the hydrolysis of the esters, but without success. The hydrolysis of the products obtained by reducing the active amyl and menthyl esters of mesaconic, α-methylcinnamic, and pyruvic acids gave rise to inactive acids. Similar negative results were obtained by *Kipping* (P. 1900, 226). *A. M'Kenzie* (J. C. S. 1904, 1250; 1905, 1373; 1906, 365) has succeeded in accomplishing several asymmetric syntheses. Thus when *l*-menthyl pyruvate, $CH_3 \cdot CO \cdot CO \cdot OC_{10}H_{19}$, is reduced by aluminium amalgam, a mixture of unequal amounts of *l*-menthyl *d*-lactate and *l*-menthyl *l*-lactate is formed. When this mixture is hydrolysed by an excess of alcoholic potassium hydroxide and the *l*-menthol removed, a dextro-rotatory potassium salt containing an excess of *l*-lactate over *d*-lactate is produced; this mixture, when acidified, becomes lævo-rotatory, and the asymmetric synthesis of *l*-lactic acid is thus accomplished. If *l*-menthyl benzoylformate, $C_6H_5 \cdot CO \cdot CO_2 \cdot C_{10}H_{19}$, is treated in exactly the same manner, the final product is *r*-mandelic acid, due, probably, to the racemizing effect of the alkali. A second asymmetric synthesis has been accomplished by *M'Kenzie* by means of *Grignard's* reaction. Thus *l*-menthyl benzoylformate and magnesium methyl iodide yield the additive compound $CMePh(O \cdot MgI)(CO_2C_{10}H_{19})$, which is converted by dilute acids into the *l*-menthyl phenylmethylglycollate $CMePh(OH)(CO_2C_{10}H_{19})$, from which, on hydrolysis with alcoholic potassium hydroxide, a lævo-rotatory potassium phenylmethylglycollate, $CMePh(OH)(CO_2K)$, was obtained. Thus



Similar active acids have been obtained by using other *Grignard* reagents in conjunction with *l*-menthyl benzoylformate. For numerous negative results see J. C. S. 1922, 351. See also *Marckwald*, B. 1904, 349.

Asymmetric synthesis takes place in the presence of enzymes, thus by combining aromatic aldehydes with hydrogen cyanide in the presence of emulsin, *Rosenthaler* (Bio. Zeits. 1909, **14,** 238; **17,** 257; *Rosenthaler*, Fer. F. 1922, **5,** 331) has prepared optically active cyanhydrins, and *Bredig* and *Fiske* (ibid. 1912, **46,** 7) have obtained similar results by effecting the combination in the presence of optically active alkaloids, *e.g.* in presence of quinine *l*-mandelo-cyanhydrin is formed, and in presence of quinidine the isomeric *d*-compound.

The Walden Inversion.—In a chemical reaction in which one radical is displaced by another, it is usually assumed that the group introduced takes the place of the radical removed, unless reasons to the contrary can be adduced. When an optically active compound is used we should expect the product formed to correspond in configuration with the original substance. That this is not always true follows from the fact that during certain reactions racemization occurs, and the product obtained is optically inactive (cf. p. 266). Even more remarkable than this is the phenomenon known as Walden's inversion. An example of this is met with in the conversion of *l*-chloro-succinic acid into the *d*-isomeride by the following series of reactions:

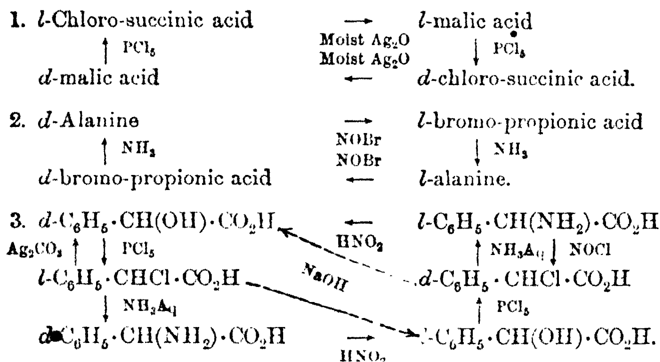


It is not possible to say which of the two reactions is normal and which abnormal, as although the malic acid may be lævo-rotatory, its configuration may correspond with that of the *d*-chloro-acid and not with that of the *l*-acid.

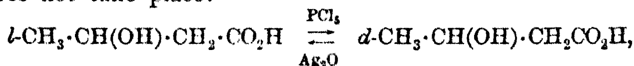
Walden (B. **32,** 1833) carried out a remarkable series of experiments on the reaction between *l*-chloro- and *l*-bromo-succinic acids and various alkalis. He found that the hydroxides of potassium, rubidium, and ammonium gave practically pure *d*-malic acid, moist silver oxide gave the pure *l*-malic

acid; and the hydroxides of sodium, barium, lead, and lithium gave mixtures in which the *d*-acid preponderated, whereas oxides of mercury and palladium gave mixtures in which the *l*-acid was in excess. The conclusion was drawn that the reaction with potassium hydroxide is normal, and that inversion occurs when silver oxide is used.

Interesting cases are those in which a complete cycle is involved, *e.g.*:

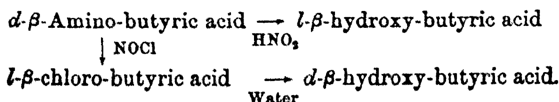


Practically all the inversions mentioned above occur when the asymmetric carbon atom has a carboxyl group attached to it. Experiments made by *E. Fischer* and *Scheibler*, with compounds in which the asymmetric atom is in the β-position with respect to the carboxylic group, prove that inversion does not take place:

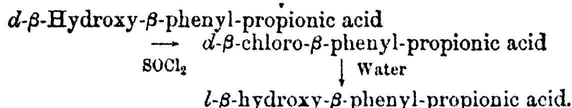


and similar results are obtained when the methyl esters are used. The same holds good in the case of β-hydroxy-β-phenyl-propionic acid (*M'Kenzie* and *Humphreys*). There are, however, several exceptions, *e.g.*:

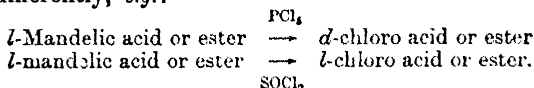
1. *Fischer:*



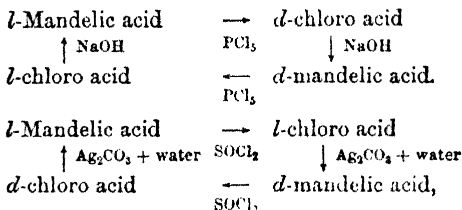
2. *M'Kenzie and Barrow:*



Frequently phosphorus pentachloride and thionyl chloride react differently, *e.g.*:



In connection with this the following cycles are of interest.



and generally the reaction with $SOCl_2$ followed by Ag_2CO_3 produces inversion, but whether this occurs in the first or second stage it is difficult to say. Impurities in thionyl chloride can bring about intramolecular change (M. 1913, **34**, 561; Bull. Soc. 1913, **13**, 229).

Inversion also takes place in compounds containing no COOH or COOR group.

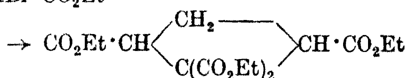
(For details see *Walden*, B. **28**, 2772; **29**, 133; **30**, 3146. *E. Fischer* and students, B. **41**, 889, 2891; **42**, 1219, **43**, 2020; A. **381**, 123; **383**, 337; **386**, 374. *Werner*, A. **386**, 65. *M'Kenzie* and others, J. C. S. 1908, 811; 1909, 777; 1910, 121, 473, 1016, 1355, 2564; 1911, 1910, 1912, 390; 1913, 687; 1914, 1583; 1915, 702, 1685.)

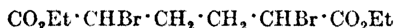
Senter and others (J. C. S. 1915, 638; 1916, 1091; 1918, 140, 151; 1924, 2137; 1925, 1847) have studied the effects of various solvents on the inversion in the case of ammonium phenylchloroacetate, $C_6H_5 \cdot CHCl \cdot COONH_4$, when Cl is replaced by NH_2. They find that there is change of sign with 6 solvents, and no change with 6 others. The latter include water and benzonitrile, and the former liquid ammonia and acetonitrile. In the case of the replacement of Br by NH_2 in α-bromo-

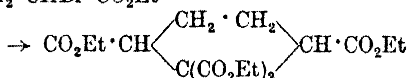
phenylpropionic acid there is always change of sign of rotation whichever solvent is used, and at the same time appreciable racemization. Replacement of OH by Br in $OH \cdot CHPh \cdot CH_2 \cdot CO_2H$ produces the same bromo acid in all solvents.

A change in configuration during ring closure has been observed by *Perkin* and others (J. C. S. 1921, 1393; 1924, 1492). Thus the esters of the $\alpha\alpha'$-dibromoglutaric and adipic acids exist in *meso* and *dl* forms, under the influence of sodio ethyl malonate ring closure takes place, and an ester of a tetracarboxylated cyclobutane or cyclopentane is formed



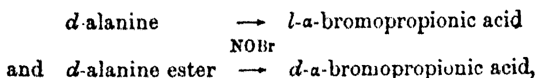






If no inversion occurs the *meso* bromo derivative should yield the *meso* tetracarboxylic ester in both cases and similarly the *d-l* bromo-compound should yield the *d-l* cyclic esters. In reality it is found that starting with either pure *meso* or pure *d-l* bromo-compound the product is a mixture of *meso* and *d-l* cyclic esters.

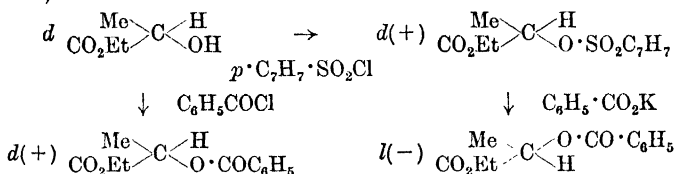
Numerous attempts have been made to ascertain in which particular reactions inversion occurs, *e.g.* whether by NaOH or Ag_2CO_3 or moist oxide in the replacement of halogen by OH, and whether by $SOCl_2$ or PCl_5 in replacement of OH by Cl. *Walden* argued that the reaction with strong alkalis which are largely ionized would probably be one of direct displacement, and hence not a case of inversion; the reaction with silver oxide would therefore be a case of inversion, and could be accounted for by the formation of an additive compound with the metallic hydroxide and subsequent removal of metallic chloride. *Fischer* by comparing the reactions:



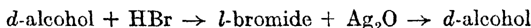
argued that inversion is less liable to occur with an ester than with an acid, and hence the first reaction represents an in-

version. Subsequent experiments by *M^cKenzie* have shown that inversion can occur with esters, as ethyl α-phenyl-lactate yields chloro esters of different signs when treated with PCl_5 or $SOCl_2$. In 1913 *Frankland* (J. C. S. 1913, 738) stated that "there does not exist at the present time any criterion whereby the relations between the configuration of an optically active compound and that of a derivative can be decisively ascertained."

An interesting case of inversion occurs during the formation of the benzoyl derivative of ethyl *d*-lactate using two different methods (*Kenyon*, *Phillips*, and *Turley*, J. C. S. 1925, 399):



It is claimed that the only reaction in which inversion can occur is the one in which potassium benzoate is involved, as in the other two reactions the C·O· union must remain intact. *Housa*, *Kenyon*, and *Phillips* (1929, 1700) developing this method in the case of *d*-β-octanol, $C_6H_{13}\cdot CHMe\cdot OH$, and its derivatives have shown that the *d*-alcohol yields *d*(+) octyl *p*-toluenesulphinates and *d*(+) *p*-toluenesulphonates $R\cdot CHMe\cdot O\cdot SOC_7H_7$ and $R\cdot CHMe\cdot O\cdot SO_2C_7H_7$; when the toluenesulphonate is heated with potassium acetate a (−) β-octyl acetate is formed, this must involve inversion as the *d*-alcohol directly acetylated yields the *d*-acetate. Also the *d*-*p*-toluenesulphinate with HOCl yields the *l*-alcohol and with chlorine the (−) chloride. The first of these reactions definitely involves a Walden inversion and therefore probably the second also. The changes



d-alcohol + HBr → *l*-bromide + Ag_2O → *d*-alcohol

therefore probably involves two Walden inversions and the authors state that inversion occurs whenever a group attached to an asymmetric carbon atom is replaced unless a phenyl group is attached to this atom or a carboxyl group is present in the molecule.

Clough, 1918, 526; 1926, 1674) has subsequently discussed

the whole question, and has settled, with a fair amount of certainty, whether inversion does or does not occur in certain particular cases; cf. however, *Kuhn* and *Wagner-Jauregg*, B. 1928, 504; *Freudenberg* and *Lux*, 1083.

1. Starting with *Freudenberg's* conclusion (B. 1914, **47**, 2037) that the four hydroxy acids, *l*-lactic, *l*-glyceric, *d*-malic, and *d*-tartaric all possess the same relative configurations, that is to say, the H, OH, and CO_2H radicals attached to the asymmetric carbon atoms have a similar spatial disposition in the molecules of these compounds,* he shows that all four acids show well-defined regularities when their rotatory powers or those of their derivatives are compared. Thus in all cases the effect of rise in temperature is to increase dextro-rotation or diminish lævo-rotation, the effects of dilution are similar, and the presence of inorganic salts produces similar effects, thus sodium bromide tends to diminish positive rotation, and even to change the sign, but to increase negative rotation. With *l*-malic acid, which has the enantiomorphous configuration, the effect of sodium bromide is to change a negative to a strongly positive rotation. He then argues that any other α-hydroxy acid which behaves similarly to the above-mentioned four acids, when the effects of temperature, dilution, solvent, and mineral salts are studied, must necessarily have a similar configuration, and any α-hydroxy acid which behaves in the opposite manner must have the enantiomorphous arrangement. Based on this argument, it is shown that *l*-lactic, *l*-glyceric, *d*-malic, *d*-tartaric, *d*-α-hydroxybutyric, *l*-α-hydroxyisovaleric, *d*-α-hydroxyisohexoic, *d*-α-hydroxy-β-phenylpropionic, and *d*-α-hydroxyglutaric acid and their derivatives all possess the same relative configurations, and for the sake of convenience the prefix "*d*" is used to denote this configuration.†

2. Similar methods have been used in the case of α-amino

* Freudenberg's conclusion is based on the fact that these compounds can be transformed into one another by reactions which do not involve displacement of groups directly attached to the asymmetric carbon atom; and, as so far no example is known in which such a change produces inversion, it is justifiable to assume that in these reactions no change in configuration occurs.

† Thus *l*-lactic acid is denoted as "*d*" lactic acid since its configuration is similar to that of *d*-malic acid and of other acids belonging to the "*d*" series. It is best represented as *d*(−) lactic acid, denoting that it is laevorotatory although belonging to the *d*-series.

acids, and the conclusion is drawn that the following naturally occurring acids all possess the same relative configurations:—*d*-alanine, *l*-serine, *l*-aspartic acid, *d*-valine, *l*-leucine, *d*-isoleucine, *d*-α-aminobutyric acid, *d*-glutamic acid, *l*-phenylalanine, and *l*-tyrosine. The configuration is denoted by "*l*". The conclusion that *l*-serine and *d*-alanine have similar configurations has been proved by *Fischer* and *Raske* (B. 1907, **40,** 3717) by transformations which do not involve the displacement of groups directly attached to the asymmetric carbon atom.

3. In a similar manner it is concluded that all the dextrorotatory α-halogenated acids are configuratively similar compounds.

4. By a careful examination of the rotatory powers of the optically active α-chloroacylamino acids, $R \cdot CH(CO_2H) \cdot NH \cdot CO \cdot CHClR'$, and α-aminoacylamino acids, $R \cdot CH(CO_2H) \cdot NH \cdot CO \cdot CHR' \cdot NH_2$, the conclusion is drawn that the $\cdot COCHR \cdot NH_2$ and $\cdot CO \cdot CHRCl$ group have very similar effects, and hence the acids from which these groups are derived have similar configurations; in other words, the α-amino acids of the "*l*" series mentioned in section 2 have configurations similar to the *d*-halogen acids of section 3. If this is so, then in the great majority of cases the conversion of an amino acid into a halogenated acid by means of nitrosyl chloride or bromide is usually accompanied by inversion, as *d*-alanine gives *l*-bromopropionic acid, and *l*-leucine gives *l*-α-bromoisohexoic acid.

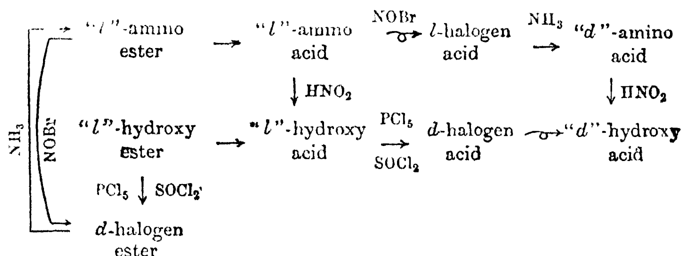
The following scheme represents the usual relationships between α-amino fatty acids and their esters and the α-halogenated fatty acids, where the straight arrows indicate direct exchange and the ⟶ an inversion.

d-α-halogen acid	⇄	*d*-α-halogen ester
↓ NH_3		$NOBr$ ↑ ↓ NH_3
"*l*" α-amino acid	⇄	"*l*"-α-amino ester
↓ $NOBr$		
l-α-halogen acid	⇄	*l*-α-halogen ester
↓ NH_3		$NOBr$ ↓ ↑ NH_3
"*d*"-α-amino acid	⇄	"*d*"-α-amino ester

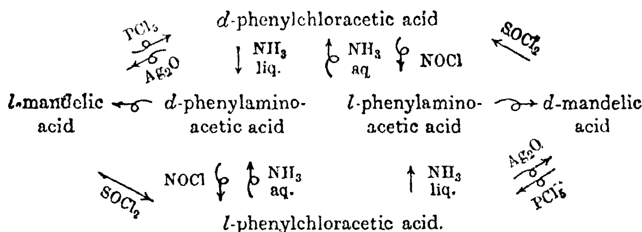
The exceptions are "*l*" valine and "*l*" isoleucine, and in these cases the action of ammonia on the free bromo acids is abnormal.

Since the effect of inorganic salts on the rotatory powers of "*l*"-alanine, *l*-aspartic acid, *l*-glutamic acid, *l*-lactic acid, and *l*-malic acid is similar in each case, it is argued that these compounds are configuratively similar. Hence the action of nitrous acid on active aliphatic α-amino acids is normal or consists in direct replacement.

It follows from the above that the *d*-halogen acids are constituted similarly to the "*l*" hydroxy acids. Hence:

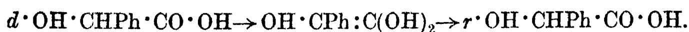


and in the mandelic acid series:



For theories of Walden inversion cf. *Fischer*, A. 1911, **381**, 123; 1912, **386**, 374; *Werner*, B. 1911, 873; *Biilmann*, A. 1912, **388**, 330; *Gadamer*, Chem. Z. 1912, **36**, 1327; *Rördam*, J. C. S. 1928, 2447; 1929, 1282; *Holmberg*, B. 1926, 125.

Racemisation.—The most likely explanation of the readiness with which α-carboxylic acids undergo racemisation (p. 266, 722) is to be found in the possibility of the tautomeric change:



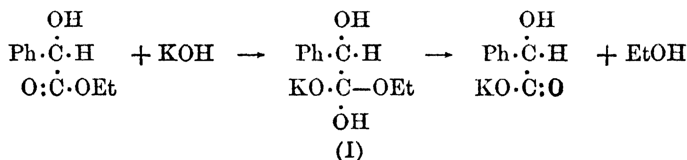
$$d\cdot\mathrm{OH\cdot CHPh\cdot CO\cdot OH} \rightarrow \mathrm{OH\cdot CPh{:}C(OH)_2} \rightarrow r\cdot\mathrm{OH\cdot CHPh\cdot CO\cdot OH}.$$

The asymmetry of the molecule is destroyed by enolisation,

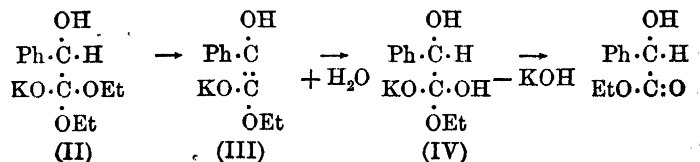
and thus on the reformation of the carboxylic group and the production of an asymmetric carbon atom equal amounts of the *d* and *l* compounds will be formed. This view is supported by the fact that *l*-atrolactic acid, $OH\cdot CPhMe\cdot CO_2H$, which contains the carboxylic group attached to the asymmetric carbon atom but which cannot undergo tautomeric change owing to the absence of the necessary hydrogen atom is remarkably stable and does not exhibit the phenomenon of racemisation (see *M^cKenzie* and *Widdows*, J. C. S. 1915, **107**, 702).

Closely related to the above are the phenomena observed on hydrolysing the esters or amides of optically active acids with alkalis (*M^cKenzie* and *Wren*, J. C. S. 1919, 602; 1922, 1348). When aqueous sodium hydroxide is used, little or no racemisation occurs, and the resulting acid is optically active; with alcoholic potash, which always contains a certain amount of potassium ethoxide, distinct racemisation takes place, and if the saponification is incomplete, the unsaponified ester has undergone racemisation to a greater extent than the acid formed.

In both cases the first stage in hydrolysis is probably an additive reaction at the carbonyl group: with aqueous potash KOH is the addendum, and with alcoholic potash KOEt. Thus with ethyl *l*-mandelate in aqueous solution the additive compound (I) immediately breaks up into the



l-potassium salt and ethyl alcohol; at no stage is the grouping around the asymmetric C atom disturbed. In alcoholic solution the additive compound (II) is optically active;



but by the elimination of alchohol gives an unsaturated inactive compound (III), which adds on water and loses KOH, yielding a mixture of equal amounts of *d* and *l* esters, as the re-formation of the asymmetric C atom in (IV) is a synthesis from a compound previously devoid of one, and therefore results in the formation of equal amounts of optical antipodes. The inactive ester in its turn is hydrolysed to inactive acid. The additive compound (IV) is identical with (I), except that it is the *d*-*l*-form, and the reason why it decomposes into KOH and ester rather than into potassium salt and alcohol is probably due to the presence of the large excess of alcohol which would prevent the dissociation in that particular direction.

Ketones of the type MePhCH·CO·Ph are readily racemised in the presence of alkali, probably owing to enol formation (J. C. S. 1926, 779).

J. Electrical Conductivity

Attention has previously (p. 167) been drawn to the fact that the degree of ionization, a, of an acid in solutions of given concentration, v, may be determined by a comparison of the electrical conductivity, λ (reciprocal of resistance), at that dilution with the conductivity at infinite dilution when ionization would be complete, *i.e.* $a = \frac{\lambda}{a \propto}$. From *Ostwald's* dilution law, based on the law of mass action, it follows that $\frac{a^2}{v(1-a)}$ is a constant $= k$, where $v =$ number of litres of solution containing one equivalent of acid. This constant k (or $100\,k =$ K) is known as the dissociation constant, and is used as a measure of the strength of all feeble acids. The effect of the introduction of strongly negative groups into the acid molecule on this constant has been referred to (pp. 173, 479), and the influence of strongly positive groups, *e.g.* NH_2, is equally marked. Thus benzoic acid = 0·006, *o*-amino-benzoic = 0·0009, *m*-amino-benzoic = 0·0010, and *p*-amino-benzoic = 0·008.

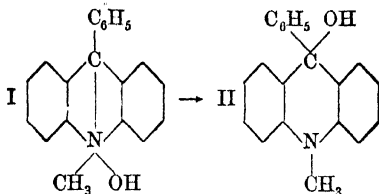
Hantzsch has used the electrical conductivity method in the diagnosis of pseudo-acids and bases. Thus with certain nitro-compounds the ordinary compound $R·CH_2·NO_2$ is a pseudo-acid and the isonitro-compound R·CH:NO·OH is a true acid,

and all the salts are derived from the latter. These salts, as a rule, are but little hydrolysed, as the isonitro-compounds are relatively strong acids. A solution of such a salt will thus contain the metallic ions and the isonitro-ion $R\cdot CH\colon NO\cdot \bar{O}\cdot$. When this solution is mixed with an equivalent quantity of hydrochloric acid the ions present are $\overset{+}{Na}$, $\bar{Cl}$, $R\cdot CH\colon NO\cdot \bar{O}\cdot$, and $\overset{+}{H}$. In the majority of cases there a considerable tendency for the strongly acidic and hence strongly ionized isonitro-compound (true acid) to become transformed into the ordinary nitro-compound (pseudo-acid). As this is practically a non-electrolyte, it follows that as this transformation occurs the conductivity of the solution will gradually diminish until it attains the value of a sodium chloride solution of the given concentration. Thus with sodium *p*-bromophenylnitromethane, $C_6H_4Br\cdot CH\colon NO\cdot ONa$, at 25°, and $v = 256$, after mixing with an equivalent of hydrochloric acid, the conductivity, $\mu = 151{\cdot}4$ after 1·5 minute, and after 45 minutes a constant value $\mu = 129{\cdot}5$ was obtained. This approximates to the value $\mu_{256} = 114{\cdot}4$ for sodium chloride, and the difference may be due to secondary changes.

This reaction has been studied in detail by *Branch* and *Jaxon-Deelman* (J. A. C. S. 1927, 1765) in methyl alcoholic solution. After an initial disturbance due to the rapid formation of a comparatively weak electrolyte in equilibrium with its ions, one of these ions becomes involved in a slow unimolecular change resulting ultimately in the complete production of the pseudo acid. The changes are represented Aci derivative $\rightleftharpoons \overset{+}{H}$ + ion of aci derivative which is rapid, the ion then changes slowly into the ion of the pseudo acid, and this reaction is practically nonreversible, and finally the ion of the pseudo acid unites with a hydrogen ion rapidly by means of a covalency yielding the unionised pseudo acid.

For optically active nitro compound and sodium salt of isonitro compound see *Kuhn* and *Albrecht*, B. 1927, 1297.

Similar results have been obtained with pseudo-bases. The true base, methyl-phenyl-acridonium hydroxide (I), which is first liberated when salts of the base are decomposed with alkali, is readily transformed into the pseudo-base with the carbinol formula (II):



which is practically a non-electrolyte. When a solution of the chloride of the base is neutralized with an equivalent of sodium hydroxide, the solution has a maximum conductivity which gradually diminishes until the value for a solution of sodium chloride of the given concentration is practically reached. Similarly with the sulphate and an equivalent quantity of barium hydroxide; at 0° and $v = 256$, the initial conductivity was $\mu = 119{\cdot}2$, but after 15 hours it has fallen to $\mu = 1{\cdot}7$ (due to small amounts of dissolved barium sulphate). Phenomena of this kind, which are termed by *Hantzsch* " slow neutralization ", are largely used to denote tautomeric change, *i.e.* the change from a true acid to a pseudo acid or from a true base to a pseudo-base (cf. pararosaniline, p. 519, cotarnine pp. 602, 748) during the conversion of the salt into the acid or base. Cf. *Madelung*, J. pr. 1925 [II], **111**, 100; 1926, **114**, 1; 1927, **115**, 24.

For **thionium** pseudo bases see *Hartley* and *Smiles*, J. C. S. 1926, 1821; 1927, 534.

The study of other physical properties such as **Internal Viscosity** (Zeit. phys. 1887, **1**, 285, 293; 1888, **2**, 744; compare also *Dunstan* J. C. S. 1907, 1728; 1908, 1815, 1919; 1909, 1556; 1910, 1935), **Heat of Combustion** (*Stohmann*, Zeit. phys. 1890, **6**, 334; 1892, **10**, 410), **Capillary Constants** (*Schiff*, A. 1884, **223**, 47), **Magnetic Susceptibility** (*Pascal*, Bull. 1909, 1110; 1910, 17, 45; 1911, 6, 79, 134, 177, 336, 809, 868) indicate that here also there are similar relationships between constitution and physical properties. **Tesla Luminescence Spectra** (*Stewart*, J. C. S. 1923, 642, 817, 2147; 1924, 1743; 1925, 999; 1926, 17; 1929, 2401, 2407, 2432, 2436. By using the high-tension Tesla discharge it is possible to photograph the emission spectra of highly complex compounds such as benzene and its derivatives. That of benzene is remarkably regular, and most of the spectra are highly constitutive in character, although conjugation appears to have little effect.

The X-ray Examination of crystals by *Bragg* and others has proved extremely valuable in the study of inorganic compounds. It has also been applied to the study of solid carbon compounds in order to throw light on the spatial arrangements of atoms within the molecule. The results confirm many of the fundamental conceptions of organic chemistry.

Thus the examination of solid methane supports the tetrahedral arrangement of the hydrogen atoms around the central carbon, and indicates that for most purposes the four valencies are equivalent. (P. R. S. 1929, A. **122,** 69.) Also benzene appears to have a plane formula, as the study of hexamethylbenzene shows that all six carbon atoms lie in one plane, with, however, only a centre of symmetry (Trans. F. S. 1929, 356). Naphthalene derivatives also have a plane formula (P. R. S. 1928, A, **118,** 709) whereas cyclohexane derivatives, *e.g.* $C_6H_6Br_6$, have three-dimensional formulæ, probably puckered hexagons, J. A. C. S. 1928, 764. On the other hand the examination has thrown light on the arrangement of the atoms within complex co-ordination molecules, *e.g.* basic beryllium acetate, $OBe_4(C_2H_3O_2)_6$ (P. R. S. 1923, A. **104,** 437).

The chain in the series of homologous monobasic acids is zigzag \/\/\/, at any rate after the first few members of the series, whereas in the compounds $C_6H_5{\cdot}C{:}C{\cdot}C{:}C{:}C{\cdot}C{\cdot}C_6H_5$ it is probably |_|¯|_|¯| . For relations between infra-red absorption and *Raman* effect, see Ind. J. P. 1928, 1930.

XLVIII. FERMENTATION AND ENZYME ACTION

A. Alcoholic Fermentation

Lavoisier, 1789, was the first to recognize that alcoholic fermentation consists essentially in the decomposition of a sugar into alcohol and carbon dioxide; and *Gay-Lussac*, 1810, drew attention to the fact that the presence of air appeared to be essential for fermentation and putrefaction to take place. The fact that brewers' yeast is a low form of plant life was discovered independently by *Cagnaird-Latour*, *Theodor Schwann*, and *Kützing*, 1837. By microscopical examination they observed the growth of the organism, and showed that it could be destroyed by heat or by certain poisons. These results were not accepted by *Berzelius*, *Liebig*, and others, who still regarded yeast as a chemical substance without life. According to *Berzelius* the yeast acted as a contact substance which decomposes the sugar without undergoing change itself: whereas *Liebig* regarded the ferment as an extremely susceptible substance, which undergoes a change of the nature of decay, and suggested that the decomposition of the sugar was a type of sympathetic reaction induced by the change of the ferment. In 1857 *Pasteur* began his researches on fermentations. He was able to show that in other cases of fermentation, such as the lactic fermentation of milk, micro-organisms are present. He was further able to show that during alcoholic fermentation the yeast grows and multiplies, and was led to the conclusion that fermentation is a physiological process accompanying the life of the yeast.

In his own words: "I am of opinion that alcoholic fermentation never occurs without simultaneous organization, development, multiplication of cells, or the continued life of cells already formed". This conclusion harmonized with the facts already known that boiled liquids could be kept from fermenting by heating or filtering through cotton wool the air admitted to the liquid.

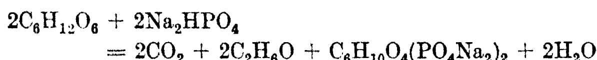
It was *Pasteur* who proved that only 95 per cent of the glucose is accounted for as carbon dioxide and alcohol; he was able to isolate glycerol and succinic acid from the final products.

As early as 1858 *M. Traube* expressed the view that all fermentations produced by living organisms are ultimately

due to ferments, which are definite chemical substances manufactured in the cells of the organism. These ferments he regarded as analogous to proteins. *Traube's* conclusions have been verified in the case of alcoholic fermentation by *Büchner's* isolation of " zymase " from yeast (see p. 80). Büchner's yeast juice, when quite free from yeast cells, can ferment solutions of glucose, fructose, sucrose, and maltose; and the fermenting power is not destroyed by the addition of chloroform, benzene, or sodium arsenite, antiseptics which inhibit the action of living cells; by filtration through a Berkefeld filter; by evaporation to dryness at 30°–35°, or by precipitation with alcohol. The fermenting power is, however, completely destroyed by heating to 50°, or by the addition of powerful antiseptics. The activity of the juice diminishes in the course of time, as a digestive enzyme is also present which gradually decomposes the zymase. Both in rate of fermentation and in the total fermentation produced, the extract or juice is much less efficient than the equivalent amount of living yeast, and glycerol is formed as a by-product when the extract is used. During fermentation a portion of the sugar is converted into a compound of less reducing power which is not fermented, but which yields sugar when hydrolysed with acids. Permanent preparations containing zymase can be obtained by evaporating the juice to a syrup at 20°–25°, drying at 35°, and then exposing to sulphuric acid in a vacuum desiccator. Such a powder when dry retains its activity for twelve months, and can be heated at 85° for eight hours without any serious loss of fermenting power. Another preparation can be obtained by bringing the juice into 10 volumes of acetone, centrifuging, washing the precipitate with acetone and then with ether, and drying over sulphuric acid. An important medicinal preparation known as *zymin* is manufactured by stirring moist yeast with acetone, filtering and draining at the pump, again mixing with acetone and draining. The product is then roughly powdered, kneaded with ether, filtered, drained, and spread on filter paper or porous plates, and finally dried at 45° for twenty-four hours. This product is quite incapable of growth or reproduction, but produces fermentation and is much more active than yeast extract.

The researches of *Harden* and *Young* (Abs. 1905, ii. 109; 1906, i. 470) indicate that the activity of yeast juice or extract is due to an enzyme and a co-enzyme, which can be

separated by filtration or dialysis through a Martin gelatin filter; the residue contains the enzyme and the filtrate or dialysate the co-enzyme. Neither by itself can induce fermentation, but a mixture of the two is equal in activity to the original juice. The co-enzyme is dialysable, and is not destroyed by boiling, but disappears from yeast juice during fermentation, or when the juice is allowed to undergo autolysis. It cannot be a protein, and its nature has not yet been determined. It is decomposed by acid or alkaline hydrolysing agents, by repeatedly boiling the extract, and also by the lipase of castor beans. In the case of other fermentations brought about by enzymes, *e.g.* lipase, it has been demonstrated that both enzyme and co-enzyme are necessary, and also that the co-enzyme is a salt of the complex taurochloric acid (p. 203). *Harden* and *Young* (Abs. 1908, i. 590; Bio. J. 1927, 1216) have also shown that phosphates added to a mixture of glucose and yeast juice produce both an initial acceleration and also an increased total fermentation. An optimum concentration of phosphate exists which produces a maximum initial rate of fermentation; an increase beyond this optimum diminishes the rate. The reaction between the glucose and phosphate is represented by the following equations:—



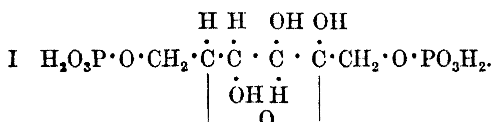
$$2C_6H_{12}O_6 + 2Na_2HPO_4 = 2CO_2 + 2C_2H_6O + C_6H_{10}O_4(PO_4Na_2)_2 + 2H_2O$$



and $$C_6H_{10}O_4(PO_4Na_2)_2 + 2H_2O = C_6H_{12}O_6 + 2Na_2HPO_4.$$

According to the first a hexose-diphosphoric acid is formed, and this is then hydrolysed by the water and yields sodium phosphate, which can then react with a further quantity of glucose. These conclusions are supported by the following facts. Careful experiments have shown that during the period of increased fermentation the amounts of alcohol and carbon dioxide produced exceed those which would have been formed in the absence of added phosphate by a quantity exactly equivalent to the phosphate added in the ratio $C_2H_6O:Na_2HPO_4$. (Compare also *Iwanoff*, Abs. 1909, **1**, 752.) It has been proved that the metallic phosphate is not the co-enzyme already mentioned, as the filtered enzyme and phosphate are not capable of inducing fermentation in the absence of the filtrate. Fermentation does not proceed in the absence of phosphate although both

enzyme and co-enzyme are present, and although arsenates and arsenites have accelerating actions on the rate of fermentation they cannot be used in place of the phosphate. The function of the arsenate or arsenite appears to be to act as accelerators in the decomposition of the glucose phosphate. *Slator* finds that phosphates have not an accelerating effect when living yeast cells are employed. He has estimated (J. C. S. 1906, **89**, 128; 1908, **93**, 217) the amounts of carbon dioxide evolved during given periods of time when yeast itself is used, and finds that the rate of fermentation is exactly proportional to the amount of yeast present, and is almost independent of the concentration of the glucose. A hexosediphosphoric acid (see previous page) and also a monophosphoric acid occur naturally in yeast, and similar, if not the same, compounds are met with in muscle extract and in blood. They appear to be of great importance in animal and plant metabolism. The compounds present in yeast have been shown to be γ-fructose-1:6-diphosphoric acid (*I*) and trehalose monophosphoric acid (*Robinson* and *Morgan*, Bio. J. 1928, 1270):



Other complex phosphoric acids play an important part in animal physiology, two of these have been isolated, viz. creatinephosphoric acid and argininephosphoric acid; they are generally termed **Phosphagens.** The latter is hydrolysed on contraction of a muscle and is reformed during the aerobic recovery phase.

A yeast which can ferment glucose does not necessarily ferment an isomeric sugar, *e.g.* galactose; it is probable that different enzymes are required for the different sugars.

The fermentation of glucose undoubtedly consists of a whole series of chemical reactions; at present we know the substances we start with and the final products obtained. Several suggestions have been made with regard to the nature of some of the intermediate products. *Büchner* and *Meisenheimer* (B. 1905, **38**, 620) have suggested that lactic acid (p. 221), a product also formed in muscle tissue by oxidation of the sugar glycogen, is first formed by the action of zymase on glucose,

and that a second enzyme, lactacidase, then decomposes the lactic acid into ethyl alcohol and carbon dioxide; cf. Bio. Z. 1922, **128,** 144; **132,** 165. This suggestion was based on the fact that a concentrated solution of glucose with alkali yields about 3 per cent of alcohol on exposure to sunlight, whereas a more dilute solution under similar conditions gives a 50-per-cent yield of lactic acid.

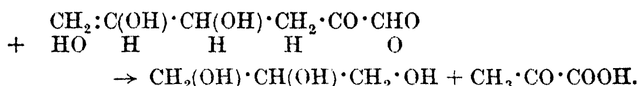
Another suggestion is that dihydroxy-acetone, $CO(CH_2 \cdot OH)_2$, is an intermediate product, and it has been proved that this compound can be fermented by yeast (*Büchner* and *Meisenheimer*, B. **43,** 1773; *Lebedew*, **44,** 2932); compare also *Franzen* and *Steppuhn*, ibid. 2915. The formation of dihydroxy-acetone and glyceraldehyde from *d*-fructose is readily explicable, as the latter is formed by the condensation of the former compounds under certain conditions (p. 325), and in all probability the reaction is a reversible one. It has also been suggested that glyceraldehyde, by the loss of water, yields the enolic form of methyl-glyoxal, $CH{:}C(OH) \cdot CHO$, and from methyl-glyoxal either lactic acid or even alcohol and CO_2 can be formed by the addition of water. That compounds like glyceraldehyde, methyl-glyoxal, or lactic acid are important intermediate products in the process of alcoholic fermentation appears to be highly improbable in view of the fact that the first of these is only slowly fermented, and the last two are unacted upon by yeast and yeast juice (*Slater*, and *Büchner*, and *Meisenheimer*).

Neuberg, 1911, has shown that yeast contains an enzyme, **carboxylase,** which is capable of eliminating CO_2 from α-ketonic acids, and suggests that pyruvic acid (p. 233) is an intermediate product in the formation of alcohol, the carboxylase decomposes the pyruvic acid into acetaldehyde and CO_2, and the aldehyde is reduced by the yeast to ethyl alcohol. It has been proved that the addition of pyruvic acid to the fermenting liquor in the presence of glycerol, which may act as an enzyme preservative, increases the yield of alcohol, and it is also known that yeast contains enzymes capable of reducing aldehydes (p. 685). The link which is missing is the conversion of a hexose into pyruvic acid.

Neuberg and *Arinstein* (Bio. Z. 1921, **117,** 269; **122,** 307) suggest that the fermentation occurs in the following stages:

(1) Glucose $- 2H_2O \rightarrow$ methylglyoxal-aldol $CH_3 \cdot CO \cdot CH(OH) \cdot CH_2 \cdot CO \cdot CH{:}O$ which can react in its enolic form, $CH_2{:}C(OH) \cdot CH(OH) \cdot CH_2 \cdot CO \cdot CHO$.

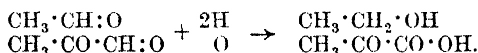
(2) The aldol, or two mols. of methylglyoxal, by the addition of water yield glycerol (1 mol.) and pyruvic acid (1 mol.).



$$\begin{array}{l} CH_2{:}C(OH){\cdot}CH(OH){\cdot}CH_2{\cdot}CO{\cdot}CHO \\ +\ HO\quad H\quad H\quad H\quad O \\ \rightarrow CH_2(OH){\cdot}CH(OH){\cdot}CH_2{\cdot}OH + CH_3{\cdot}CO{\cdot}COOH. \end{array}$$

Part of the pyruvic acid yields alcohol under the influence of carboxylase and a reductase.

(3) A molecule of methylglyoxal and a molecule of acetaldehyde can yield a molecule of alcohol and of pyruvic acid by the addition of $H_2 + O$.



$$\begin{array}{l} CH_3{\cdot}CH{:}O \\ CH_3{\cdot}CO{\cdot}CH{:}O \end{array} + \begin{array}{l} 2H \\ O \end{array} \rightarrow \begin{array}{l} CH_3{\cdot}CH_2{\cdot}OH \\ CH_3{\cdot}CO{\cdot}CO{\cdot}OH. \end{array}$$

The actual formation of acetaldehyde during fermentation can be proved by adding a compound which can fix aldehydes, *e.g.* bisulphite or dimethyldihydroresorcinol.

Alcoholic fermentation can take place in three different ways according to conditions:

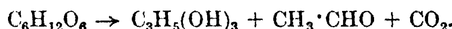
(*a*) Normal in fairly acid media, over 90 per cent yields



$$C_6H_{12}O_6 \rightarrow 2C_2H_5{\cdot}OH + 2CO_2.$$

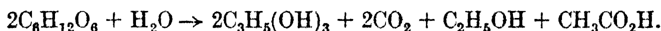
probably through stages suggested by *Neuberg*.

(*b*) In presence of sulphites



$$C_6H_{12}O_6 \rightarrow C_3H_5(OH)_3 + CH_3{\cdot}CHO + CO_2.$$

(*c*) Under feebly alkaline conditions, *e.g.* in presence of $NaHCO_3$

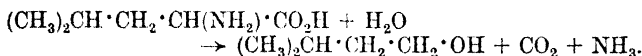


$$2C_6H_{12}O_6 + H_2O \rightarrow 2C_3H_5(OH)_3 + 2CO_2 + C_2H_5OH + CH_3CO_2H.$$

The objection raised that acetaldehyde and pyruvic acid are not so readily fermented as glucose has lead *Neuberg* to suggest that these may be fermented in one of their tautomeric (*e.g.* enolic) forms.

Of the by-products mentioned on p. 79, glycerol is formed from the sugar, as *Büchner* and *Meisenheimer* have shown that it is also formed when yeast extract or zymin acts on sugar solutions. As stated on p. 205, the yield of glycerol can be increased to 25 per cent or more of the weight of the sugar by using suitable yeasts in the presence of sodium carbonate or sulphite. The fusel oil and succinic acid, on the other hand,

do not owe their origin to the sugar, but to other products present in the mixture undergoing alcoholic fermentation. The researches of *F. Ehrlich* (1904–10) prove that the alcohols and also the aldehydes present in ordinary fusel oil are derived from the amino-acids formed by the hydrolysis of proteins. Thus isoamyl alcohol, one of the chief constituents of fusel oil, is closely related to leucine, α-amino-isohexoic acid, and active amyl alcohol to isoleucine, α-amino-β-methyl-valeric acid, both of which are formed by the hydrolysis of proteins, and according to *Ehrlich* both these acids are transformed into the corresponding amyl alcohols under the influence of pure yeast cultures, in the presence of sugar:



$$(CH_3)_2CH\cdot CH_2\cdot CH(NH_2)\cdot CO_2H + H_2O \rightarrow (CH_3)_2CH\cdot CH_2\cdot CH_2\cdot OH + CO_2 + NH_3.$$

These changes, although brought about by yeast, do not occur when zymin or yeast extract is used. Other amino acids undergo a similar decomposition: tyrosine (p. 489) yields *p*-hydroxy-phenyl-ethyl-alcohol, tryosol, $OH\cdot C_6H_4\cdot CH_2\cdot CH_2\cdot OH$, and phenyl-alanine (p. 483) gives phenyl-ethyl alcohol.

The ammonia is not found at the end of the reaction, as it is used up by the organism for the purpose of building up new protein molecules. If appreciable amounts of simple nitrogenous substances, such as ammonium salts, are originally present in the fermenting liquor, the organism uses these in preference to decomposing the amino-acids; and *Ehrlich* has found it possible to increase or diminish the amounts of fusel oil formed, by diminishing or increasing the amounts of ammonium salts present at the beginning of the fermentation, and also to increase the fusel oil by the addition of larger amounts of amino-acids to the fermenting mixture. (Cf. Chap. LVI, Rubber.) Practically all amino-acids formed by the hydrolysis of proteins can undergo similar decomposition by yeast, but only in the presence of sugar. The succinic acid found as a by-product in alcoholic fermentation is probably formed in a similar manner from glutamic acid.

According to *Neuberg* and *Fromherz* (1911), ketonic acids are probably formed as intermediate products in the fermentation of amino-acids to alcohols; and *Neuberg* has been able to show that many α-ketonic acids, *e.g.* pyruvic, $CH_3\cdot CO\cdot CO_2H$, and oxalacetic, $CO_2H\cdot CH_2\cdot CO\cdot CO_2H$, are readily decomposed by yeast even in the absence of sugar, yielding carbon

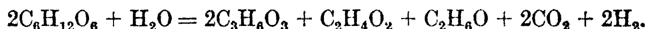
dioxide and aldehyde. (Cf. p. 785.) With a 1-per-cent solution of pyruvic acid the decomposition is almost as rapid as with a sugar solution. For summary of work on yeast growth and fermentation cf. *Slator*, J. S. C. I, 1919, **38**, 391 R.

For fermentations induced by organisms other than yeasts, see pp. 156, 158, 222. A fermentation of considerable commercial value is the butyl alcohol fermentation of starch or carbohydrates, usually maize mash, by means of a bacterium termed **clostridium acetobutylicum.** The products are *n*-butyl alcohol, acetone, carbon dioxide and hydrogen and the proportions roughly those represented by the equation:



$$3C_6H_{12}O_6 \rightarrow 2C_4H_9{\cdot}OH + (CH_3)_2CO + 7CO_2 + 4H_2 + H_2O$$

the primary products are probably acetic and butyric acids and oxygen which oxidizes the butyric to acetoacetic acid and hydrogen or the simultaneous oxidation and reduction of two molecules of butyric acid by $2H_2O$, *i.e.* 4H + 2O. (For details of process see Ind. Eng. 1927, **46**, 1147.) Steaming stable manure contains a bacillus which is capable of attacking most forms of cellulose under either anaerobic or aerobic conditions at temperatures between 35° and 70°. The products vary with the conditions and include acetic, butyric and lactic acids, alcohol carbon dioxide and methane. According to *Harden* (J. C. S. 1901, 610) *Bacillus coli communis* ferments glucose, fructose, or mannitol, yielding lactic, succinic, and acetic acids, alcohol, formic acid, carbon dioxide, and hydrogen. The main reaction can be represented by the equation:



$$2C_6H_{12}O_6 + H_2O = 2C_3H_6O_3 + C_2H_4O_2 + C_2H_6O + 2CO_2 + 2H_2.$$

With glucose the weight of lactic acid is practically 50 per cent of the sugar, and the alcohol and acetic acid are formed in equal amounts. The alcohol probably comes from the group $(CH_2(OH){\cdot}CH(OH)$, and as this group occurs twice in the molecule of mannitol the yield of alcohol is much greater when this compound is used. The lactic acid is probably derived from the $CH(OH){\cdot}CH(OH){\cdot}CH(OH)$ grouping. *B. typhosus* yields similar products, except that it gives formic acid instead of carbon dioxide and hydrogen (Abs. 1906, II, 380).

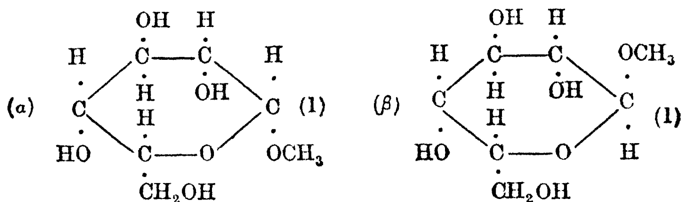
The mould, **aspergillus niger,** is a useful ferment for the production of acids, *e.g.* citric and oxalic from sugars, and *Chal-*

lenger and others have made a systematic study of the changes and also of the action of the organism on intermediate products (J. C. S. 1927, 200, 3044; 1929, 1644, 1987, 2485).

B. Enzyme Action

Attention has been drawn several times (pp. 79, 80, 452) to the fact that chemical decompositions can be brought about by certain complex organic substances found in animal and plant tissues. Such substances are termed *unorganized ferments* or *enzymes*. The great majority act as catalysts in processes of hydrolysis, *e.g.* invertase which hydrolyses cane sugar, amylase which hydrolyses starch, emulsin (p. 452), myrosin (p. 649), pepsin and trypsin (p. 657); *lipases* which hydrolyse glycerides; and *esterases* which hydrolyse esters; but in addition there are enzymes which bring about oxidation, viz. the *oxidases*; enzymes which reduce aldehydes to alcohol, the *reductases*; enzymes which eliminate CO_2 from acids *carboxylases* (p. 785); enzymes which produce clotting, *e.g.* *thrombase* the blood-clotting enzyme, *rennin*, which produces the clotting of milk, and *pectase* which acts upon the pectins of plants; enzymes which bring about complex reactions, *e.g.* zymases. The enzymes are unstable nitrogenous compounds of colloidal nature, but not necessarily proteins. They act as catalysts, in the majority of cases as positive, but in a few as negative. The catalytic nature is shown by the fact that the rate of reaction is directly proportional to the concentration of the enzyme, but that the total decomposition is independent of the amount of enzyme, provided sufficient time is allowed, and provided the enzyme does not undergo decomposition; as a rule a small amount of the enzyme cannot decompose unlimited amounts of substrate (the substance which is decomposed), as most enzymes are relatively unstable and can readily undergo proteolytic decomposition, and if only a small amount of enzyme is used the reaction slackens and finally ceases, owing to the autolysis of the enzyme, before all the substrate is decomposed. They are sensitive to high temperatures, *e.g.* when heated to below 100° their activity is completely destroyed; they are, however, resistant towards certain antiseptics which destroy protoplasm and kill fermenting organisms. Strong antiseptics, such as formaldehyde, tend to destroy enzymes. Enzymes are often precipitated from their colloidal solutions

by the addition of alcohol or acetone, but such products are not pure; in many cases they consist of a mixture of enzymes, and in this way the study of their reactions is complicated. The modern system of nomenclature is to name the enzymes according to the compounds they hydrolyse, *e.g.* maltase, sucrase (= invertase), amylase (= diastase), &c. The nature of the products formed varies not merely with the substance used, but also with the enzyme; thus the trisaccharose, raffinose, if hydrolysed by acids, yields galactose, fructose, and glucose; the same carbohydrate with diastase yields melibiose and fructose, and with emulsin galactose and sucrose. The action of enzymes is essentially **selective**, and in this respect differs from the hydrolysing action of alkalis or acids. Thus esters, amides, carbohydrates, glucosides, &c., are all hydrolysed by hydrochloric acid; whereas esters, but not carbohydrates, can be hydrolysed by lipases, and maltose, but not sucrose, can be hydrolysed by maltase. Even a slight difference in the configuration of two isomeric substances is sufficient to affect their reactivity with a particular enzyme, *e.g.* the two methyl-glucosides (p. 646), which are represented by the spatial formulæ:



the only difference being the arrangement of the H and OCH_3 attached to the carbon atom (1). Of these two compounds the *a* can be hydrolysed by maltase but not by emulsin, and the *β* by emulsin but not by maltase, and hence the names *a* and *β* glucase are sometimes used for the two enzymes maltase and emulsin. So specific are the activities of the hydrolysing enzymes that practically each di-, tri-, or poly-saccharose has its own enzyme, which frequently accompanies it in the plant or animal tissue. The enzyme does not always exist as such in the tissue; sometimes it is present as a zymogen which forms the enzyme in presence of a suitable reagent, usually an acid.

Inulase hydrolyses inulin; cellulase (or cytase) cellulose; lactase, lactose; melibiase, melibiose, &c.

Similarly, each of the natural glucosides described on pp. 646–651 is accompanied in the plant by its own enzyme; and as most of them are hydrolysed by emulsin but not by maltase, they are regarded as analogous to the β-methyl-glucoside, with complex radicals in place of the methyl group. Maltose on the other hand is an α-glucoside resembling the α-methyl compound in configuration. Invertase is probably a mixture of two enzymes, one of which is attracted to the glucose and the other to the fructose portion of the sucrose molecule. A biose need not necessarily be hydrolysed to a monose before fermented by yeast, since maltose can be fermented by maltase free yeast. Alkylglucosides derived from non-fermentable sugars, *e.g.* pentoses and heptoses are not attacked by either α or β glucase.

Numerous other examples of the same type have been met with, especially in the case of polypeptides (*Fischer* and *Bergell*, B. **36**, 2592; **37**, 3103).

Among the proteolytic enzymes the following are the commonest (see *Willstätter*, J. C. S. 1927, 1359; B. 1926, 1): (*a*) Erepsin; (*b*) Trypsin; (*c*) Pepsin.

(*a*) **Erepsin** from pancreas juice hydrolyses polypeptides but not proteins.

(*b*) **Trypsin** also from pancreatic secretion hydrolyses peptones and simple proteins but not casein or gelatin, but when activated by enterokinage will hydrolyse these latter. Trypsin acts best in alkaline solution, and usually produces amino-acids and tri- and tetrapeptides (p. 655), and in addition can hydrolyse many synthetical polypeptides, especially those derived from amino-acids of high molecular weight, but its action is selective as it will not hydrolyse glycylalanine, also *d*-alanyl-*d*-alanine is hydrolysed, but *d*-alanyl-*l*-alanine is not.

(*c*) **Pepsin** present in the gastric secretion acts best in presence of 0·2 per cent hydrochloric acid, also secreted by the mucous membrane. It is a protein of high molecular weight, has no action on synthetic polypeptides, but hydrolyses proteins to proteoses, peptones, and amino-acids.

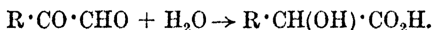
Enzymatic synthesis of proteins can be accomplished by means of pepsin (J. Bio. C. 1924, **62**, 15, 633, 675; **63**, 563, 575). Thus it will act on a concentrated solution of the products of

the peptic digestion of egg albumin giving a product of the order of complexity of the original protein.

Other enzymes derived from the animal body are: arginase, which converts arginine into ornithine and urea; guanase, which converts guanine into xanthine; and adenase, which converts adenine into hypoxanthine; the first occurs in the liver and kidney, and the last two in the spleen, thymus, and liver. Animal muscle contains an enzyme which produces lactic acid from glycogen and as carbohydrate mono- and di-phosphoric acids appear to be intermediate stages in this degradation; there is close analogy with yeast fermentation.

Glutathione (p 661), a dipeptide derived from cystine and glutamic acid, and present in yeast and animal tissues, is an important factor in oxidative changes and forms a mechanism capable of taking up esters, hydrogen or oxygen and thus assisting in processes of oxidation or reduction, and thus plays an important part in the biochemistry of the cell. *Urease* transforms urea into ammonium carbonate by the addition of water.

Glyoxalase is an enzyme present in tissues and secretions, and is capable of converting glyoxals into hydroxy acids:



$$R \cdot CO \cdot CHO + H_2O \rightarrow R \cdot CH(OH) \cdot CO_2H.$$

Tyrosinase and *laccase* are examples of oxidases, and they often occur together. The former oxidizes tyrosine (α-amino-β-p-hydroxyphenyl-propionic acid, $OH \cdot C_6H_4 \cdot CH_2 \cdot CH(NH_2)$ CO_2H, to homo-gentisic acid, 2:5-dihydroxyphenylacetic acid, and then to an insoluble black product. Both are capable of oxidizing polyhydric phenols. Laccase occurs in the juice of the lac tree, and oxidizes the juice to a black product. *Catalase* is the name given to various enzymes present in animal and vegetable tissues, and their characteristic property is the readiness with which they destroy hydrogen peroxide. *Peroxidases* are enzymes which activate hydrogen peroxide, and thus bring about actions which the peroxide alone is incapable of effecting. For classification of oxidases see *Pugh* and *Raper*, Bio. J. 1928, 274.

It has been proved in many cases that a particular enzyme can act not merely as a hydrolysing but also as a synthesising agent. The process of hydrolysis is frequently a balanced reaction, although in the majority of cases the equilibrium is mainly in the direction of analysis and not synthesis. The

synthesising activity of an enzyme was first demonstrated by *Croft-Hill* (J. C. S. 1898, 634; 1903, 578) in the case of maltase. The greater portion of the maltose is hydrolysed to glucose, but a certain proportion of disaccharose is always present, and in a solution of glucose maltase can produce a certain amount of a disaccharose, **revertose**, which at first was thought to be maltose, but has since been proved to be isomeric (*Georg* and *Pictet*, Helv. 1926, 612). Invertase, lactase, emulsin, and lipases have all been shown to possess synthetical activity. The formation of starch in plant and glycogen in animal tissues is probably largely due to the activities of synthesising enzymes; and *Pottevin* has succeeded in synthesising a triolein, one of the common constituents of natural fats, by means of a lipase.

Bourquelot and his co-workers (Annales, 1913 (viii), **28**, 145) have synthesised numerous β-glucosides and β-galactosides by means of β-glucase (emulsin). As the reaction is reversible, it is advisable to reduce the amount of water and to work in the presence of an appreciable excess of alcohol or other hydroxylic compound which is to form the glucoside with the dextrose. The following β compounds have been synthesised:—Methylglucoside, geranylglucoside, cinnamylglucoside, and benzylglucoside, most of which are definite crystalline compounds which are readily hydrolysed by β-glucase in the presence of water. α-Glucosides and galactosides have been synthesised by means of an enzyme (α-glucase) present in the aqueous extract from bottom yeast (ibid. 1915 [ix], **3**, 28), and α- and β-glucosides and galactosides derived from di- and tri-hydric alcohols, *e.g.* glycol and glycerol have also been prepared (ibid. **4**, 310).

Emulsin not only contains β-glucase but also other enzymes, *e.g.* gentiobiase, cellase, and β-galactase (C. R. 1915, **161**, 463). The best yields of β-alkylglucosides are obtained by using solutions containing about 15–20 per cent of dextrose. With higher concentrations of dextrose and smaller concentrations of alcohol the effects of the gentiobiase and cellase become apparent, and by the action of emulsin on an aqueous solution of *d*-galactose it has been found possible to isolate a syrupy galactobiose with $\alpha_D = +54°$ (ibid. C. R. 1916, **163**, 60).

The action of invertase (sucrase) on cane sugar appears to be a non-reversible one, and hence the synthesis of sucrose from *d*-glucose and *d*-fructose by this enzyme is not to be

expected (*Hudson*, J. A. C. S. 1914, **36**, 1571; Lob. Abs. 1916, i, 296).

It is now generally conceded that a particular enzyme which produces the hydrolysis of a glucoside is the enzyme which is instrumental in synthesising that glucoside, as the same equilibrium is attained when the reaction is started from either end (C. R. 1913, **156**, 957; *Bayliss*, P. R. S. 1912, B. **85**, 359).

The rate of hydrolysis by means of enzymes has been studied by different authorities. Many, *e.g.* *O'Sullivan* and *Thompson* (J. C. S. 1890, 834) and *Hudson* (J. Am. C. S. 1908, 1160, 1564; 1909, 655) indicated that in the inversion of sucrose by invertase constant values for K, can be obtained by using the ordinary equation for a unimolecular reaction, provided that the complications attending the mutarotation of the glucose and fructose (p. 763) are avoided by adding a small quantity of alkali before taking the polarimetric reading. The alkali stops the inversion, and at the same time rapidly brings about equilibrium between the α- and β-glucoses and the α- and β-fructoses, so that the normal rotatory power of invert sugar is given. *Hudson's* results clearly prove that the α-modifications of glucose and fructose are first formed. Compare *Rosanoff*, *Clerk*, and *Selby*, J. A. C. S. 1911, **33**, 1911.

Other results (*Armstrong*, P. R. S. 1904, 1907, 1908, 1910, 1912, 1913) show that if the products of action are removed and no deterioration of enzyme occurs the amount of decomposition per unit time is constant throughout the change, *i.e.* the hydrolysis-time curve is linear, and this agrees with the conclusion that enzyme and substrate form definite compounds.

A view generally held with regard to the mechanism of enzyme reaction is that adsorption of substrate by the enzyme, followed in some cases by activation at certain centres or even by combination, takes place. The fact that a specific enzyme can hydrolyse only particular substrates is in harmony with this view, as it is known that chemical constitution plays an important part in adsorption. Cf. *H. E.* and *E. F. Armstrong*, P. R. S. 1913, B. **86**, 561.

In living tissues a number of complex substances are present which are capable of interfering with the action of an enzyme. These are termed anti-enzymes. Some are normally present

in tissue, others appear to be formed when an enzyme is injected into the tissue.

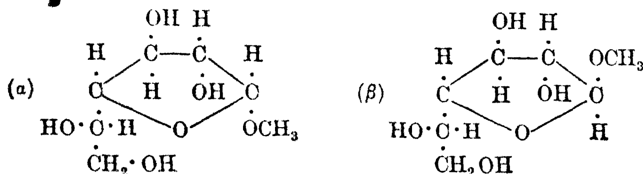
The hydrogen ion concentration of the substrate is an important factor in enzyme reactions, for each enzyme an optimum hydrogen ion exists and is denoted by P_H.

For pure water $H' = OH' = 1 \times 10^{-7 \cdot 07}$ ions per litre, i.e. the P_H for pure water is 7·07.

If the H' concentration of a liquid is greater than that of water the liquid is acid and if less it is alkaline. For acid media the value of P_H can lie between 7·07 and 0, and for alkaline media from 7·07 to 14·14.

C. Mono- and Poly-Saccharoses

For many years it was customary to represent the α- and β-methylglucosides (p. 790) and hence the α- and β-glucoses, the equilibrium mixture of which is present in an aqueous solution of glucose after the elapse of several hours, when mutarotation is complete, as cyclic structures containing a ring of 4 carbon atoms and 1 oxygen atom, i.e. as compounds of a butylene oxide or furane type, *e.g.*



These formulæ were first suggested by *Fischer* (B. 1893, 2400), and readily accounted for the existence of two stereochemical forms of α-methylglucoside. The selection, however, of the five-atom ring in preference to a three- or four- or six-atom ring, had no scientific basis apart from analogy with the lactones, *e.g.* *Fischer* had shown that *d*-gluconolactone (p. 315) which contains a 5-membered ring, when reduced with sodium amalgam in the presence of dilute sulphuric acid yields *d*-glucose. At one time *Nef* (A. 1914, **403**, 204) suggested that the α-glucoside has the butylene oxide (five-atom ring) structure, whereas the β-compound should be represented by an ethylene oxide (three-atom ring) structure, but *Fischer* (B. 1914, 1980) and *Michaelis* (1913, 3683) brought forward arguments against such a structure for the β-compound.

The similarities between the α- and β-compounds and their conversion the one into the other indicate that they are presumably stereo- and not structurally isomeric, a conclusion which has been supported by the isolation of a third methylglucoside, termed the γ-compound, which is much more reactive than the α- and β-isomerides. It is readily hydrolysed by acids and readily oxidized by alkaline permanganate in the cold. It readily undergoes auto-condensation, and is affected by neither α- nor β-glucase. A fourth methylglucoside, in all probability stereoisomeric, with the γ-compound has been isolated by *Irvine* and others, and four distinct crystalline ethylglucosides are known (J. C. S. 1929, 2796).

1. PYRANOSE SERIES

More recently *Drew* and *W. N. Haworth* * (J. C. S. 1926, 2303) have brought forward arguments for a six-atom ring structure (pyranose structure) for the α- and β-methylglucosides and hence for a six-atom ring structure for most of the stable forms of the common monosaccharoses. Such formulæ have an amylene oxide or 1:5 oxide structure and such names are sometimes used, but as all such compounds can be regarded as derived from the pyrane ring (cf. pyrone, p. 565), $CH_2\left\langle\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot CH_2\end{matrix}\right\rangle O$ the generic name **pyranose** has been suggested for all such sugars.

Many of the arguments used are based on a study of the methyl derivatives of the sugars, and of the corresponding monobasic acids or their lactones. These compounds have the advantage that they are stable and are characterized by well defined physical constants. One special advantage is that a fully methylated sugar or lactone cannot undergo intramolecular change, with a shifting of the oxide oxygen linking during chemical reactions. It is clear that any argument dealing with structure based on the fact that *d*-mannolactone on reduction yields *d*-mannose is largely invalidated when it is borne in mind that the opening and subsequent reclosing of the lactone ring during the change may readily give rise to an isomeric lactone, *e.g.*:



* For general review of Howarth and his collaborators' views on Sugar Chemistry, see "Constitution of Sugars", Arnold & Co., 1929.

If, however, a fully methylated lactone is employed, *e.g.* tetramethylglucono-γ-lactone,



it is clear that even if the lactone becomes hydrated and subsequently loses water a γ-lactone must be formed, as all positions with the exception of No. 4 have OMe and not OH groups attached to carbon.

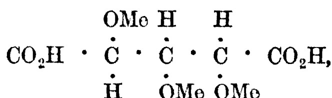
1. In 1914 *Nef* (compare also *Hedenberg*, J. A. C. S., 1915, 345) was able to obtain two isomeric lactones from *d*-gluconic acid. The ordinary or γ-lactone is readily obtained by heating the acid at 100° for a comparatively short time, and the isomeric δ-lactone is formed when the acid or its ester is heated for a prolonged period at a lower temperature. Other monobasic acids derived from aldoses yield isomeric γ- and δ-lactones, and, as a rule, the δ-form readily passes over into the more stable isomeride. A fully methylated lactone, either γ or δ, is stable and cannot undergo isomerisation. A polarimetric study of the rates of hydration of all the lactones and of their methylated derivatives, obtained by the methylation of the lactones or by the methylation of an aldose followed by oxidation, show that these lactones fall into two groups: (*a*) γ-lactones which are only slowly hydrated and (*b*) δ-lactones which are comparatively readily hydrated in aqueous solution, and thus the ease or difficulty with which any particular lactone undergoes hydration with consequent change of rotation can be utilized for ascertaining whether it belongs to the five-atom ring or the six-atom ring type. Oxidation experiments with a typical γ- and a typical δ-lactone have conclusively established the structure of the compounds. Thus the crystalline trimethylarabono-γ-lactone, m.-p. 33°, was characterized by its oxidation to 2:3-dimethoxy-4-hydroxyglutaric acid, $CO_2H\cdot CH(OMe)\cdot CH(OMe)\cdot CH(OH)\cdot CO_2H$, and the formation of this compound was accompanied by the elimination of a methoxy residue at position 5 in the carbon chain,





When the trimethyl-δ-arabonolactone was oxidized in a

similar manner with nitric acid it gave the optically active trimethoxyglutaric acid,



proving that the hydroxyl from which the lactone was derived cannot have been in position 4 (γ) but in position 5 (δ).

2. One of the strongest arguments in favour of the six-atom ring structure of the stable aldoses and ketoses is their conversion by suitable oxidizing agents into a 2:3:4-trimethoxyglutaric acid, $CO_2H \cdot CH(OMe) \cdot CH(OMe) \cdot CH(OMe) \cdot CO_2H$. It is clear that such a compound must exist in a number of stereoisomeric forms, the actual number theoretically possible is six, and each sugar gives rise to a single isomeric form, which can be identified by conversion into its amide or methylamide, $NHMe \cdot CO[CH(OMe)]_3 \cdot CO \cdot NHMe$. These are all crystalline compounds with well defined melting points. The name given to a particular trimethoxyglutaric acid is usually derived from the pentose from which it can be obtained by oxidation, *e.g.* *d*-arabotrimethoxyglutaric acid, xylotrimethoxyglutaric acid.

l-**Arabinose:** The following series of reactions are readily brought about:

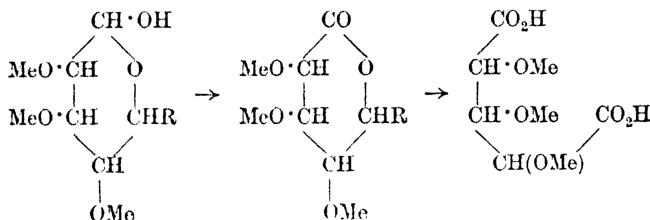
l-Arabinose $\xrightarrow{\text{MeOH+HCl}}$ α- and β-methylarabinosides $\xrightarrow{\text{completely methylated and hydrolyzed}}$ *l*-trimethylarabinose $\xrightarrow{\text{oxidized}}$ *l*-trimethylarabonic acid $\xrightarrow{\text{dehydrated}}$ *l*-trimethyl-δ-arabonolactone $\xrightarrow{HNO_3}$ *l*-arabotrimethoxyglutaric acid, the methylamide of which melts at 172°. The formation of a 2:3:4-trimethoxyglutaric acid is a clear proof that in the trimethyllactone, and hence also in the trimethylarabinose, the three methyl groups are in adjacent positions and not terminal positions, *i.e.* attached to carbon atoms numbered 1 and 5. As the reducing group which is in position 1 always takes part in the oxide ring of the aldose molecule, it follows that this oxide formation occurs at the 1:5-positions, *i.e.* it is a six-atom ring.

d-**Glucose.**—When a similar series of reactions is carried out with *d*-glucose the respective products are: α- and β-methylglucosides → tetramethylglucose → tetramethylgluconic acid

→ tetramethyl-δ-gluconolactone → xylotrimethoxylglutaric acid. The formation of this 2:3:4-trimethoxy-acid shows definitely that the oxide ring cannot engage positions 3 or 4 in the methylated aldose chain as these must be methylated, hence it must involve either position 5 or 6 of the hexose chain. The latter alternative is excluded by the fact that a 2:3:4:5-tetramethyl-gluconic acid has been definitely synthesised, and been found to differ completely from the tetramethylgluconic acid obtained by the oxidation of the tetramethylglucose. It cannot be made to pass into the tetramethyl-δ-gluconolactone and on further oxidation yields tetramethylsaccharic acid, $CO_2H[CH\cdot OMe]_4\ CO_2H$, and not a trimethoxyglutaric acid. Hence the methylated hexose must be a 1:5-oxide, *i.e.* have a six-atom ring structure, and a similar ring is presumably present in the original glucose.

Similar lines of argument have been adopted in the case of the ordinary forms of xylose, galactose, mannose, rhamnose and lyxose.

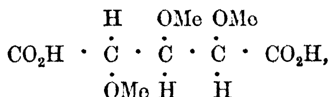
The degradation of the methylated sugar may be represented by means of the following formulæ:



R = H for a pentose and R = $CH_2\cdot OMe$ for a hexose.

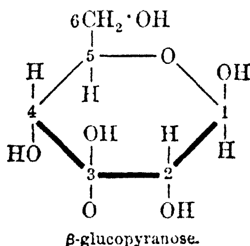
d-**Fructose.**—This is also to be regarded as belonging to the pyranose series. It yields two stereoisomeric α- and β-methylfructosides, both of which are crystalline. The β-compound is readily methylated and from the product a crystalline tetramethylfructose can be obtained. This compound is very stable when compared with the tetramethylated aldoses; bromine water is practically without action, but digestion with nitric acid converts it into a carboxylic acid, trimethylfructuronic acid, by the oxidation of a terminal $\cdot CH_2\cdot OMe$ group to CO_2H. The acid yields crystalline methyl and ethyl esters, and on further oxidation with acidified permanganate gives *d*-2:3:4-trimethyl-δ-arabonolactone, the optical enantimorph

of the lactone obtained by the action of bromine water on *l*-trimethylarabinose (p. 798) and finally *d*-arabo-2:3:4-trimethoxyglutaric acid (the enantimorph of the final oxidation product of *l*-trimethylarabinose. The formation of this dibasic acid,

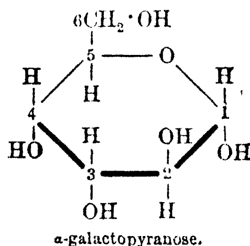


proves that the ring formation which unites carbon atom No. 2 (the carbonyl group of the open chain ketose molecule) cannot involve positions 3, 4 or 5, and must therefore be between 2 and 6, and hence *d*-fructose must contain a six-atom ring.

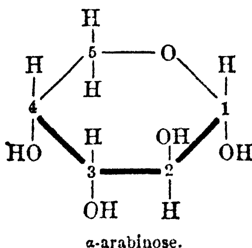
For representing the stereochemical formulæ for the cyclic monosaccharoses the method adopted for the polymethylene-carboxylic acids (p. 351) is the most convenient, *e.g.*



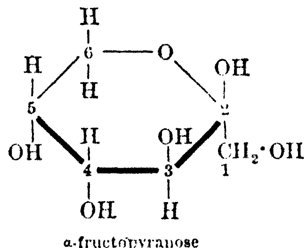
β-glucopyranose.



α-galactopyranose.



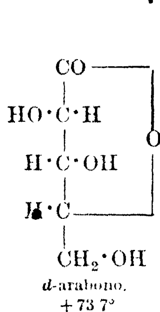
α-arabinose.



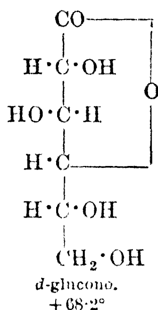
α-fructopyranose

The only differences between an α- and a β-compound is in the arrangements of the groups attached to the C atom next, in clockwise order of arrangement, to the O atom of the ring.

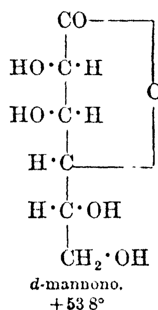
3. A confirmation of the pyranose structure of the stable monoses is found in a study of their optical rotations and *Hudson's Lactone Rule* (J. A. C. S. 1910, **32**, 338). Hudson reviewed the physical properties of some 24 crystalline lactones derived from sugars, and drew the conclusion that, using the ordinary projection formulæ (cf. p. 320) for the γ-lactones of the monocarboxylic acids derived from or related to simple aldoses, when the oxide ring of the lactone is formed by engaging an OH group on the right side of the carbon chain the optical rotation is enhanced in the dextro sense and conversely when the OH engaged is on the left of the projection formula of the acid, the optical rotation of the γ-lactone is increased in the lævo direction. A few examples are:



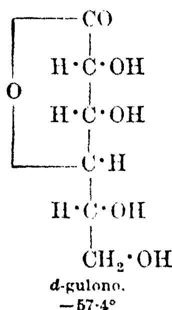
d-arabono.
+73·7°



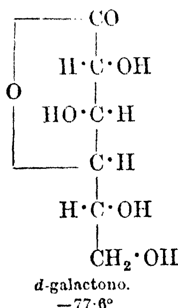
d-glucono.
+68·2°



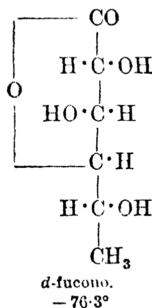
d-mannono.
+53·8°



d-gulono.
−57·4°



d-galactono.
−77·6°



d-fucono.
−76·3°

The same generalization holds good also for *Fischer's* synthetic mannoheptonolactones and mannooctonolactone. If, however, it is attempted to include in the rule the aldoses and their monomethyl ethers, with their formulæ based on a buty-

lene oxide structure, numerous exceptions are encountered. On the other hand, if they are represented with an amylene oxide or pyranose structure, complete agreement with Hudson's rule follows (*Drew* and *Haworth*, J. C. S. 1926, 2303), and so far no exception to Hudson's rule has been met with in the case of the known aldoses, their methyl derivatives and all the corresponding lactones whether γ or δ.

The spatial configurations given to the α- and β-compounds are based on the fact that, according to *Boeseken*, the presence of hydroxyl groups attached to two adjacent carbon atoms causes the hydroxyl compound to produce appreciable exaltation in the electrical conductivity of an aqueous solution of boric acid (p. 766), and the effect is still more marked if the two hydroxyls are spatially adjacent, *e.g.* on the same side of the molecule. Experiments made with the α- and β-glucoses corresponding with the α- and β-glucosides show that the α-compound produces a greater exaltation than the β-, and hence the configuration analogous to the α-methyl-glucoside represented on p. 795 is given to the α-compound, viz. the configuration in which the two OH groups attached to adjacent C atoms lie in the same plane (B. 1913, **46**, 2612). For further examples of the effect of hydroxy compounds on the electrical conductivity of boric acid cf. Abs. 1915, ii, 136, 667, 668; *Irvine* and *Steele*, J. C. S. 1915, **107**, 1221.

2. FURANOSE SERIES

Fischer's γ-methylglucoside and the two stereoisomeric γ-ethylglucosides * (p. 796) differ markedly in chemical properties from the α- and β-compounds, and are hence structurally different. Similar γ-methyl derivatives have been obtained from most of the ordinary aldoses and ketoses by adopting a method similar to that used by *Fischer*, viz. by condensing the sugar and methylalcohol *at room temperature* in the presence of 1 per cent hydrogen chloride. These γ-methylated sugars exist in two stereoisomeric forms (γ and δ) analogous to the α- and β-methyl compounds. The non-

* The four isomeric ethylglucosides may simply be termed α, β, γ, and δ, the α and β being stereoisomeric pyranose compounds and the γ and δ similarly related furanose derivatives. *Haworth* and *Porter* (J. C. S. 1929, 2796) prefer to call the α and β compounds α and β ethylglucopyranosides and the γ and δ compounds α and β ethylglucofuranosides. The melting-points and specific rotations $[\alpha]_D$ are respectively 113–114°, +150°; 73°, −33·4°; 82–83°, +98°; 59–60°, −86°.

alkylated γ-sugars have never been isolated as they are extremely labile and readily pass over into the more stable α- and β-forms (pyranose). The existence of two stereochemical forms of the labile sugar is however probable as *Schulbach* and *Huntenberg* (B. 1927, 1487) have isolated two distinct pentabenzoyl derivatives of γ-glucose. These compounds have $[\alpha]_D = +58{\cdot}6$ and $-52{\cdot}6°$. The rotations of α- and β-glucose are respectively $+110°$ and $+17{\cdot}5°$ and their pentabenzoyl derivatives $+107{\cdot}6$ and $+23{\cdot}5°$.

The five-atom ring or furanose structure originally attributed to the α- and β-methylglucosides has now been assigned (*Baker* and *Haworth*, J. C. S. 1925, 365; *Haworth* and others, 1927, 1241, 2432) to the γ-glucoside, and all labile or γ-compounds are represented by similar formulæ. So far no γ-sugar has been detected in natural products * and no indication of γ-glucose residue in any of the di- or poly-saccharoses has been adduced. On the other hand the fructose portion of cane sugar is almost undoubtedly a γ-fructose (fructo-furanose) residue (cf. p. 803).

The arguments used in favour of the furanose structure of the γ-sugars are:

1. The γ-methylglucoside when fully methylated and then hydrolysed yields a γ-tri (or tetra) methyl sugar, and when this is oxidized with bromine water a lactone is formed, which can be shown to be a γ-lactone from its relatively slow rate of hydration. Thus from γ-methylarabinoside a trimethyl γ-arabinose is formed, and this yields a crystalline trimethylarabonolactone quite different from that obtained from the α- or β-methylarabinoside, and difficult to hydrate.

γ-Methylglucoside yields a tetramethyl-γ-glucose different from the ordinary 2:3:4:6 tetramethyl compound obtained from the α- and β-methylglucosides, and with bromine water yields a γ-lactone.

2. The γ- or furanose structure of the methylated lactones is confirmed by a study of their oxidation products with nitric acid or of the oxidation products of the methylated sugars. The trimethyl-γ-arabinose on oxidation yields 2:3-dimethoxy-4-hydroxyglutaric acid. This indicates that the methyl groups are in positions 2, 3, and 5 (the last being eliminated during

* But the mutarotation of aqueous solutions of galactose indicates the presence of other substances in addition to the α and β pyranose forms, in all probability two furanose sugars.

oxidation of the CH_2·OMe to CO_2H) and the oxide ring occurs between positions 1 and 4.

$$\overset{1}{HO\cdot CH}\cdot\overset{2}{CH}(OMe)\cdot\overset{3}{CH}(OMe)\cdot\overset{4}{CH}\cdot\overset{5}{CH_2}OMe$$
(1:4-oxide ring, O linking positions 1 and 4)

$$\rightarrow COOH\cdot CH(OMe)\cdot CH(OMe)\cdot CH(OH)\cdot COOH.$$

When the corresponding 2:3:5-trimethylarabono-γ-lactone is oxidized the product is dimethyl-*d*-tartaric acid (dimethoxysuccinic acid)

$$O:\overset{1}{C}\cdot\overset{2}{CH}(OMe)\cdot\overset{3}{CH}(OMe)\cdot\overset{4}{CH}\cdot\overset{5}{CH_2}\cdot OMe$$
(1:4-oxide ring, O linking positions 1 and 4)

$$\rightarrow CO_2H\cdot CH(OMe)\cdot CH(OMe)\cdot CO_2H.$$

Fission occurs between positions 4 and 5 and CH_2·OMe is completely oxidized.

When the tetramethyl-γ-gluconolactone is oxidized it yields oxalic acid and the dimethoxysuccinic acid, and these products can only be accounted for on the basis of the 2:3:5:6-tetramethyl structure of the original compound and hence the 1:4-oxide structure of the lactone.

$$O:C\cdot CH(OMe)\cdot CH(OMe)\cdot CH\cdot CH(OMe)\cdot CH_2\cdot OMe$$
(1:4-oxide ring, O linking C and the third CH)

$$\rightarrow CO_2H\cdot CH(OMe)\cdot CH(OMe)\cdot CO_2H + CO_2H\cdot CO_2H.$$

The original sugar must also have been a 2:3:5:6-tetramethyl-derivative with a 1:4-oxide or furanose structure.

These γ-sugars or furanoses may be written:—

Tetroses.

```
HO·CH——CH·OH
   |      |
HO·CH    CH₂
    \   /
      O
```

Furanose.

Pentoses.

```
HO·CH——CH·OH
   |      |
HO·CH    CH·CH₂·OH
    \   /
      O
```

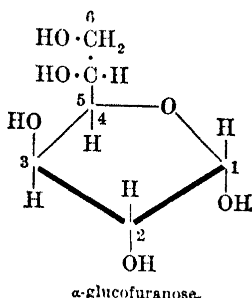
Xylofuranose,
Arabofuranose,
&c.

Hexoses.

```
HO·CH——CH·OH
   |      |
HO·CH    CH·CH(OH)·CH₂·OH
    \   /
      O
```

Glucofuranose,
Mannofuranose,
&c.

In these formulæ their relationship to furane (p. 547) is clearly seen. In the spatial formula for γ-glucose the OH



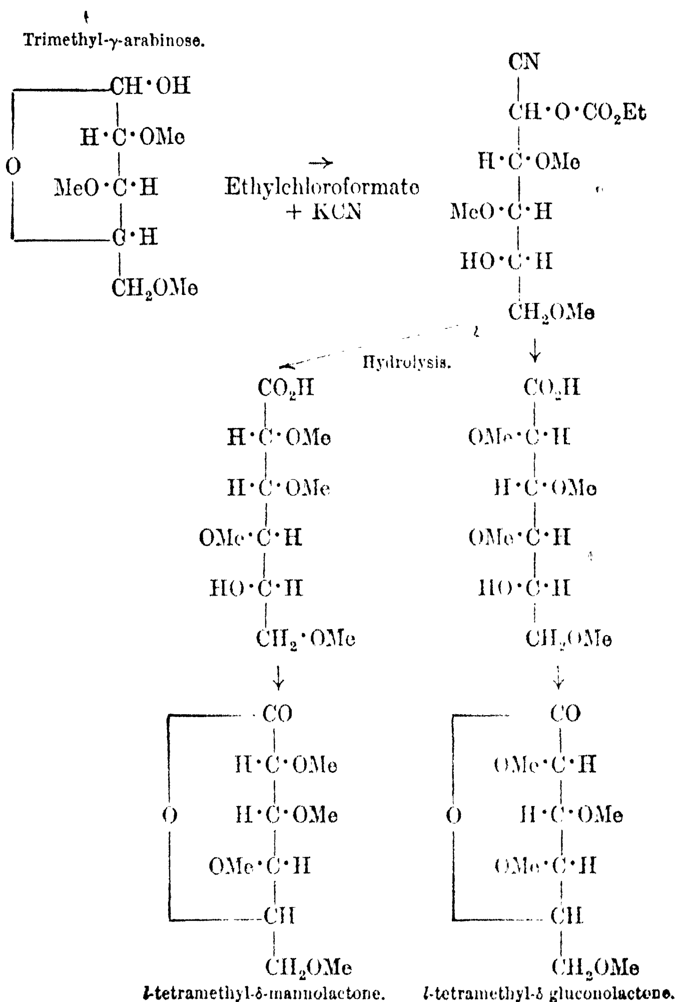
α-glucofuranose.

groups in positions 3 and 6 are fairly close and hence a change of acyl groups from position 3 to 6 can occur.

Synthesis of a hexopyranose from a pentafuranose.—Although so far it has not been found possible to synthesise a tetramethylhexose from *d*-tartaric acid, it has been found possible to synthesise *l*-tetramethyl-glucopyranose and -mannopyranose from *l*-trimethylarabofuranose by the series of reactions given on p. 806 (*Haworth* and *Peat*), and from these lactones the corresponding tetramethylated hexoses can be obtained by reduction.

3. DISACCHAROSES

The disaccharoses can be regarded as analogous to the methylglucosides, another hexose molecule playing the part of the methyl alcohol. Thus the reducing group of one molecule of hexose forms an anhydride by reacting with a hydroxyl group of a second hexose molecule, either similar to or different from the first. The second hexose group in the majority of cases retains its own reducing group intact, the condensing hydroxyl group being situated lower in the carbon chain. In a few cases, *e.g.* sucrose, the reducing group of the second hexose residue is involved in the condensation, and these bioses form the group of non-reducing disaccharoses. The former group—the reducing disaccharoses—have reducing properties, exhibit mutarotation, and yield osazones.



l-tetramethyl-δ-mannolactone. *l*-tetramethyl-δ gluconolactone.

The true structure of a biose can only be settled after the following points have been established:—

1. The nature of the monosaccharoses—whether aldoses or ketoses—taking part in the condensation. It is not only necessary to determine whether these are glucose, mannose, fructose, &c., but also whether they belong to the furanose or pyranose type, and whether the *d*- or *l*- form.

2. If the reducing group of the second hexose molecule does not participate in the union, it is necessary to fix the position of the hydroxyl group which forms the oxide.

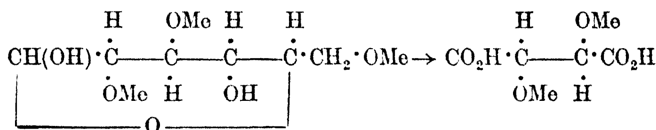
3. As the reducing group of the first hexose molecule takes part in the condensation it is necessary to ascertain if this condensation is of the type of the *α*- or of the *β*-methylglucoside, *i.e.* is the first hexose residue derived from the *α*- or *β*- form of the hexopyranose, and similarly for the second hexose residue.

For purposes of study the fully methylated, octamethyl, derivatives are generally used. These methyl derivatives are quite stable, but it has to be borne in mind that some of the dissacharoses are sensitive to alkalis, and hence in their methylation an excess of methyl sulphate should always be present, others, however, are sensitive to acid, and then an excess of alkali is necessary during methylation. Careful hydrolysis of each methylated biose molecule gives rise to two molecules of methylated monoses, which can be purified by distillation under extremely low pressures and crystallisation. In the case of the reducing sugars, one of the hexoses formed is a tetramethyl derivative and the other a trimethyl derivative * containing a free hydroxyl group, and the first stage is to determine the position of this hydroxyl in the carbon chain of the hexose.

Maltose (J. C. S. 1919, 809; 1926, 3094).—The products of hydrolysis of the syrupy octamethylmaltose (b.p. 201–203/ 0·03 mm.) are the well known 2:3:4:6-tetramethylglucopyranose, melting at 93–94° (cf. p. 798), and a trimethylglucose which has been shown to be 2:3:6-trimethylglucopyranose. The structure of the latter follows from (*a*) its conversion into the above-mentioned 2:3:4:6-tetramethyl derivative on

* One methyl group is removed during hydrolysis, viz. the one corresponding to the methyl group in the methylglucosides, *i.e.* in position 1 in the pyranose ring not united in position 1 to the second pyranose ring.

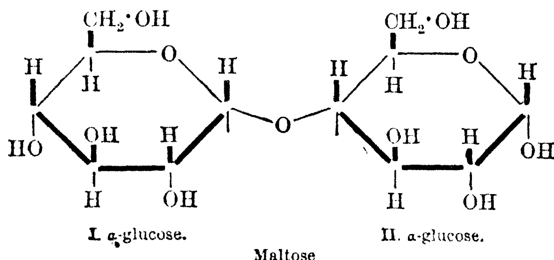
further methylation; (*b*) its oxidation to *d*-dimethyltartaric acid, $CO_2H\cdot CH(OMe)\cdot CH(OMe)\cdot CO_2H$,*



The formation of these two methylated glucopyranoses is in complete harmony with the view that both portions of the maltose molecule contain the pyranose ring, and that the union of the two involves position 1 of the one and position 4 of the other hexose molecule. Although this is probable, there is a little uncertainty as it is just possible that the portion of the molecule yielding the trimethylglucopyranose contains a furanose ring and that the biose union is between carbon atom No. 1 of the first hexose molecule and carbon atom No. 5 of the second. The initial products of hydrolysis would then be 2:3:4:6-tetramethylglucopyranose and 2:3:6-trimethylglucofuranose (a γ-sugar) and, as position 5 is not methylated, this could easily pass into the more stable 2:3:6-trimethylglucopyranose, which is the product actually isolated. The question, however, has been definitely settled by an examination of the monobasic acid, maltobionic acid, formed by the oxidation of maltose with bromine water. By this means the oxide ring in one glucose residue is ruptured by the oxidation of the reducing group. When completely methylated, first with methyl sulphate and alkali and finally with methyl iodide and silver oxide, it yields methyl octamethylmaltobionate, and the hydrolysis of this with dilute mineral acid produces hydrolysis of the ester and at the same time a cleavage of the bionic linking, and the products are:—2:3:4:6-tetramethylglucopyranose and the lactone of a tetramethylgluconic acid. Its rate of hydration shows this to be a γ-lactone and it has been proved to be identical with 2:3:5:6-tetramethyl-γ-gluconolactone, m.-p. 26°–27°. Hence it is position 4 and not 5 in the acid which has the free hydroxyl group, and hence the union of the two hexose groups in maltose is between position 1 in the first and position 4 in the second, and therefore this second group must have its oxide linking between

* The isomeric 2:3:4-trimethyl- and 2:3:6-trimethyl-glucoses do not yield dimethyltartaric acids on oxidation.

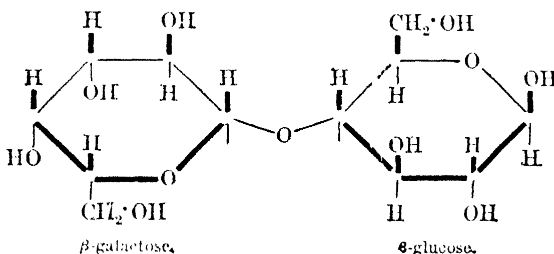
positions 1 and 5, *i.e.* it must be a glucopyranose residue. The union is of the type of α-methylglucoside as the biose is completely hydrolysed by maltase, an enzyme which is capable of hydrolysing α- but not β-glucosides.



I. α-glucose. II. α-glucose.

Maltose

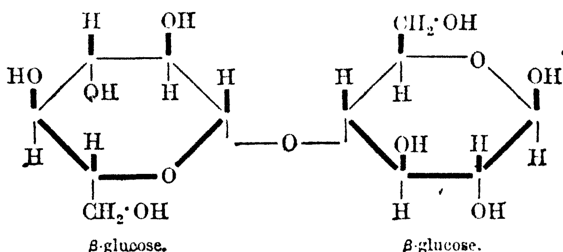
Lactose (J. C. S. 1918, 188; 1922, 1213; 1927, 544; B. 1923, 1957).—When lactose is methylated and then hydrolysed, the products are 2:3:4:6-tetramethylgalacto-pyranose, melting at 71°–72°, and the same 2:3:6-trimethylglucopyranose as is obtained from the methylated maltose, and as lactose is hydrolysed by lactase it must be a β-galactoside. Lactobionic acid, corresponding with maltobionic acid, when methylated and hydrolysed yields 2:3:4:6-tetramethylgalactopyranose and the same 2:3:5:6-tetramethyl-γ-gluconolactone as obtained from the methylated maltobionic acid. It therefore consists of a β-galactose group united in position 1 by means of oxygen to position 4 in a β-glucose residue.



β-galactose. β-glucose.

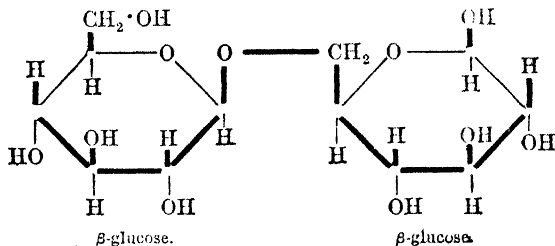
Cellobiose (J. C. S. 1921, 193; 1926, 98; 1927, 2809), an intermediate product obtained in the hydrolysis of cellulose (cf. p. 333), when investigated by the method already indicated in the case of maltose, gives identically the same tri- and tetra-

methylglucopyranoses and the fully methylated cellobionic acid (p. 331) gives the same products as methyl octamethylmaltobionic acid. As the biose is hydrolysed by emulsin, the specific for a β-glucoside, it undoubtedly consists of two β-glucose groups with an oxide linking between position 1 in the first residue and position 5 in the second.



β-glucose. β-glucose.

Gentiobiose (p. 332), (J. C. S. 1923, 3120, 3125; 1927, 1527) on methylation and hydrolysis gives 2:3:4-trimethyl- * and 2:3:4:6-tetramethyl-glucopyranose and as it is hydrolysed by emulsin contains two β-glucose residues united by oxygen in position 1 of one residue and position 6 of the other. Confirmation of this is furnished by the oxidation of the sugar to gentiobionic acid, and the hydrolysis of the completely methylated acid to 2:3:4:6-tetramethylglucopyranose and an acid proved to be 2:3:4:5-tetramethylgluconic acid, as it yields an ester but no lactone, and on further oxidation with nitric acid yields tetramethylsaccharic acid, $CO_2H \cdot [CH \cdot OMe]_4 \cdot CO_2H$.

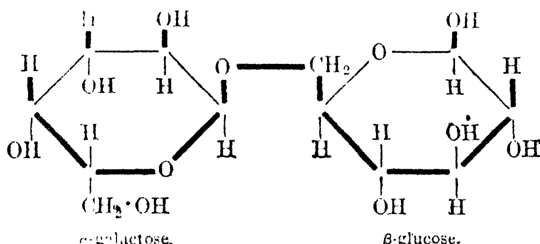


β-glucose. β-glucose.

Melibiose, one of the hydrolytic products of raffinose (p. 331), is similar to gentiobiose; its octamethy lderivative yields

* Me in position 1 is removed during hydrolysis.

2:3:4:6 - tetramethylgalactopyranose, and 2:3:4 - trimethylglucopyranose, and the completely methylated melibionic acid on hydrolysis yields 2:3:4:6-tetramethylgalactopyranose and the same 2:3:4:5-tetramethylgluconic acid as is obtained from the methylated gentiobionic acid.



It would thus appear that in trisaccharoses and in certain glucosides such as emulsin the hexose residues are united by means of oxygen between the 6th carbon atom (*i.e.* the side chain of the pyranose ring) of one residue and the first carbon of the second residue.

Further confirmation of the α- or β-glucosidic structure of the disaccharoses mentioned is obtained by a study of their optical rotations. In the following table column 1 gives the specific rotations of the methyl esters of the hexamethylmonobasic acids derived from the disaccharoses, column 2 gives the values for the mixed hydrolytic cleavage products after equilibrium is attained, and the values for the ordinary monomethyl glucosides and galactosides are:

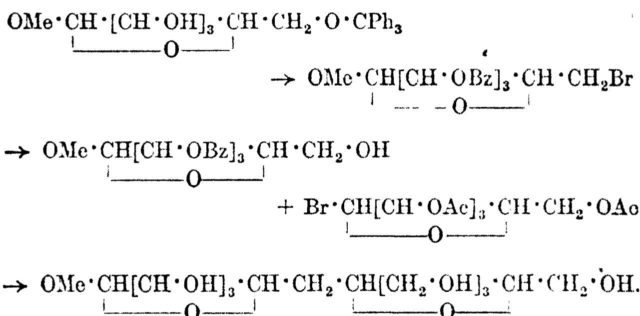
α-methylglucoside	+158°	α-methylgalactoside	+193°
β-methylglucoside	−34°	β-methylgalactoside	−1°

	1.	2.
1. Methyl octamethylmaltobionate	+121°	+55
2. Methyl octamethylmelibionate	+106°	+64
3. Methyl octamethylcellobionate	+5°	+55
4. Methyl octamethyl-lactobionate	+34°	+77

Presumably esters Nos. 1 and 2 are α- and esters Nos. 3 and 4 β-compounds. Further the reduction in the rotation value on cleavage (column 2) of Nos. 1 and 2 can be due to the change of the α-sugar (high rotation) to the equilibrium mixture of α- with β-sugar (low rotation) and the enhancement in Nos. 3

and 4 to the liberated β-sugars passing into an equilibrium mixture of α- and β-sugars (J. C. S. 1927, 3146).

Synthesis of Gentiobiose (*Helferich, Klein,* and *Schäfer,* A. 1926, **447,** 19; **450,** 225).—The starting point is 6-triphenylmethyl-α-methylglucoside, when benzoylated and treated with phosphorus pentachloride, this gives 2:3:4-tribenzoyl-6-bromo-methyl-glucoside,* m.p. 122°. From this 2:3:4-tribenzoylmethylglucoside can be obtained, and when this is condensed with 2:3:4:6-tetracetyl-1-bromo-glucopyranose and the product hydrolysed carefully to remove acyl groups methylgentiobioside is obtained.

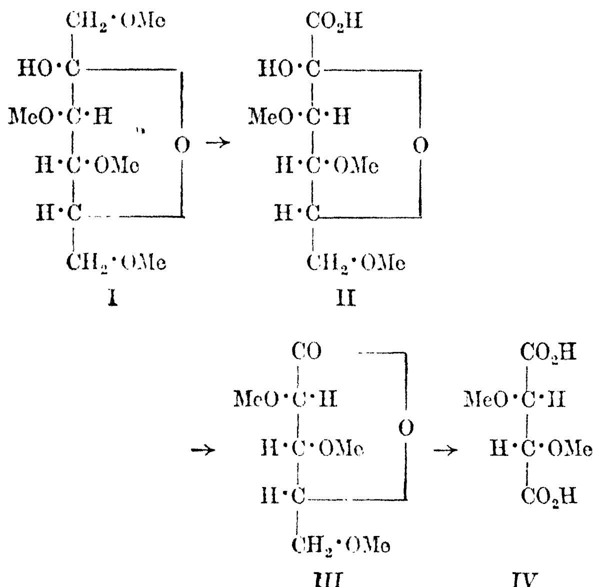


Sucrose (J. C. S. 1916, 1314; 1920, 199).—Sucrose has no reducing properties, shows no mutarotation, and does not yield an osazone. It is thus an anhydro compound in which the reducing group of each of the two components is involved. When hydrolysed the final products are *d*-glucopyranose and *d*-fructopyranose. When, however, its octamethyl derivative is hydrolysed the products are 2:3:4:6-tetramethylglucopyranose, and 1:3:4:6-tetramethylfructofuranose (I), obtained pure as a liquid with $[\alpha]_D = +31{\cdot}7°$ by hydrolysis of heptamethylsucrose after removal by distillation of trimethylglucose formed at the same time.

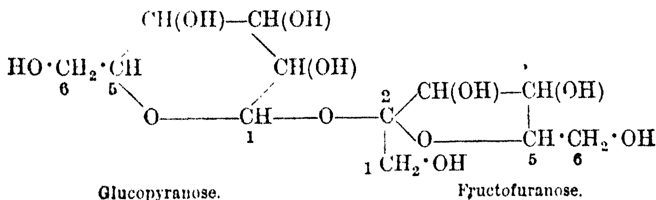
The structure of this furanose has been established:—(1) By oxidation to a trimethylfructuronic acid (II) with the elimination of a methyl group indicating the presence of a

* The structure of this follows from the fact that on reduction and hydrolysis it yields *iso*-rhamnose, $CH_3{\cdot}CH[CH{\cdot}OH]_3{\cdot}CH{\cdot}OH$.

terminal $CH_2\cdot OMe$ group. This nonobasic acid has reducing properties, showing the presence of the ketose reducing group, and this property disappears on complete methylation. (2) On further oxidation with acidified permanganate the acid yields *d*-2:3:5-trimethyl-γ-arabonolactone, (III), the optical antipodes of that obtained by oxidizing *l*-trimethylarabonofurose, and on still further oxidation with nitric acid *d*-dimethoxysuccinic (IV) acid is obtained.



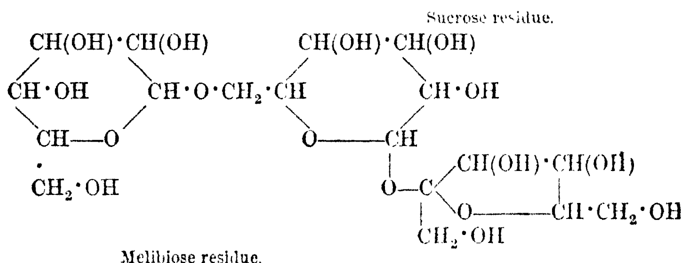
It has not yet been established with certainty whether the α or β form of each hexose is involved in the anhydride formation



Glucopyranose. Fructofuranose.

Synthesis of Sucrose (*Pictet* and *Vogel*, Helv. 1928, 436).—From the acetylation products of fructose a crystalline tetra-acetylfructopyranose and a liquid dextrorotatory tetracetylfructofuranose can be isolated, and the latter condenses with tetra-acetylglucopyranose in the presence of chloroform and phosphoric anhydride yielding crystalline octa-acetylsucrose from which sucrose is isolated by removal of the acetyl groups. Compare, however, B. 1929, 984, 1418; J. A. C. S. 1929, 1279.

Raffinose and Gentianose (J. C. S. 1923, 3125; 1927, 1527, 3146).—Raffinose on methylation takes up 11 methyl groups and on hydrolysis of the methylated product the following compounds can be isolated, 1:3:4:6-tetra-methylfructofuranose, 2:3:4-trimethylglucopyranose and 2:3:4:6-tetramethylgalactopyranose. The structure of the original sugar is hence



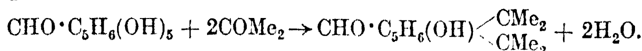
since when hydrolysed with emulsin it yields galactose and sucrose and with invertase it yields fructose and melibiose.

Gentianose is similar but contains the gentiobiose residue in place of the melibiose group.

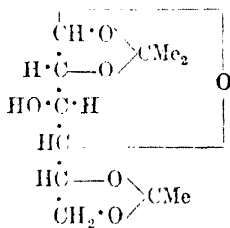
4. ACETONE COMPOUNDS OF SUGARS

The aldoses and ketoses readily condense with acetone, *e.g.* glucose-acetone and glucose-diacetone. Many of these are crystalline compounds and some can be distilled under very low pressures. They are to be regarded as isopropylidene derivatives of the sugars, the divalent isopropylidene $(CH_3)_2C$: replacing the hydrogen atoms of two hydroxyl groups in the sugar. The two hydroxyl groups are usually attached to two adjacent carbon atoms in the chain, or, if not, they must be spatially adjacent. Di-isopropylidene-glucose is obtained by

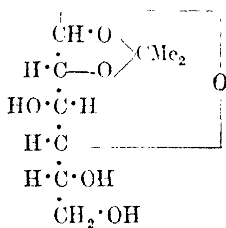
shaking an acetone suspension of glucose with a small quantity of hydrogen chloride, zinc chloride, or anhydrous copper sulphate,


$$CHO\cdot C_5H_6(OH)_5 + 2COMe_2 \rightarrow CHO\cdot C_5H_6(OH)\begin{matrix}\diagup CMe_2\\ \diagdown CMe_2\end{matrix} + 2H_2O.$$

It has no reducing properties, but contains one free hydroxyl group and yields a monomethyl ether, which, on acid hydrolysis, yields 3-methylglucopyranose. The diacetone compound on partial hydrolysis yields the monoacetone derivative, mono-isopropylidene glucose, a non-reducing compound, which on methylation and subsequent hydrolysis, yields a trimethyl glucose and this on complete methylation and oxidation yields tetramethyl-γ-gluconolactone. This proves the 1:4 oxide or furanose structure of the tetramethylglucose and hence of the original mono- and di-isopropylidene compounds.



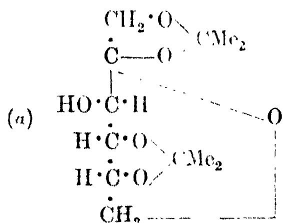
Diacetone glucose.

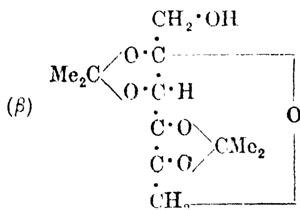


Monoacetone glucose

Cf. J. C. S. 1929, 1329, 1337.

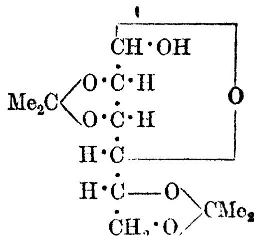
d-**Fructose** yields two structurally isomeric diacetone derivatives, both of which have been shown to be pyranose derivatives and both are non-reducing.





Mannose diacetone is interesting as it exhibits mutarotation and has reducing properties, and hence the reducing group has

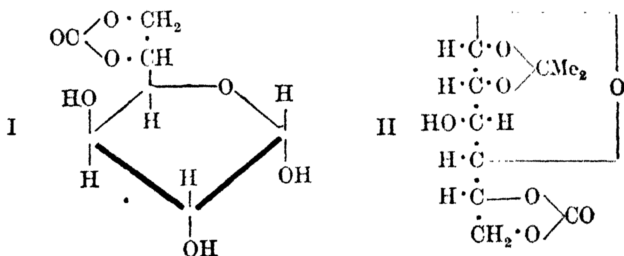
not participated in the condensation. It is represented as



i.e. a furanose although obtained from mannopyranose.

The general conclusion (*Haworth*, p. 52) based on the known reactions so far studied is that acetone residues condense with appropriately situated (structurally or spatially) hydroxyl groups in any sugar *regardless* of any preformed oxide system in the sugar. The sugar ring adjusts itself to that position (whether 4 or 5) left open after the preferential selection of positions of entry is made by the isopropylidene groups. Thus a change in ring may occur during the formation of acetone derivatives, and has actually been noted in the cases of *d*-glucopyranose, *d*-mannopyranose and *d*-xylopyranose, which yield furanose isopropylidene derivatives. With *d*-fructopyranose and *d*-galactopyranose no such change occurs. The usual position of the hydroxyl groups affected is in the *cis* position and attached to two adjacent carbon atoms, but this is not invariably true as in xylopyranose the hydroxyl groups attached in position 3 and 5 condense with acetone.

Sugar carbonates (*Haworth* and *Porter*, J. C. S. 1929, 2796; 1930, 151).—Similar to the acetone compounds are the sugar

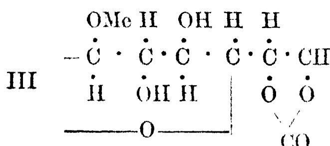


carbonates, obtained by condensing the sugars with carbonyl chloride in pyridine or mildly alkaline solutions. They are

crystalline compounds and unlike the acetone compounds they are unstable to alkalis but much more stable to acids.

The glucofuranose carbonate I is interesting as being the first definite glucofuranose derivative with the free reducing groups to be isolated.

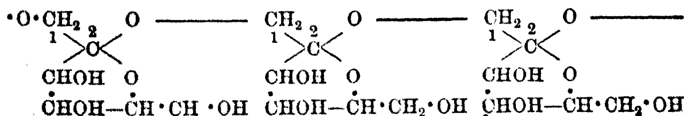
A mixed derivative, glucose-acetone-carbonate II, is formed when a glucose suspension in acetone is treated with carbonyl chloride. It forms large crystals, m.-p. 143°–145° and $[\alpha]_D - 64°$. Digestion with dilute acid in the presence of methyl alcohol eliminates the isopropylidene group and introduces methyl yielding the carbonate of methylglucofuranoside III.



5. POLYSACCHAROSES

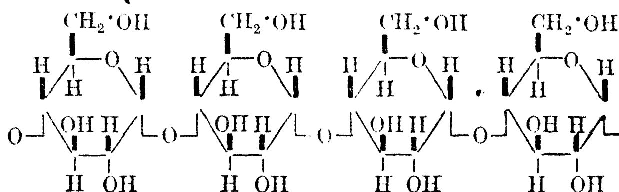
No generally accepted structures can be given for the polysaccharoses. Views differ as to the manner in which the mono- or bi-ose residues are linked in the polysaccharoses, *e.g.* whether by residual or ordinary valencies (*Hess* and *Trogus*, B. 1928, 1982; *Pringsheim*, 1926, 3008; *Haworth* and *Learner*, J. C. S. 1928, 621; Helv. 1928, 548; *Freudenberg* and *Braun*, A. 1928, **460**, 288; *Staudinger*, A. 1929, **474**, 155, 232, 259.

Inulin appears to break down when boiled with water as its mol. weight diminishes from 4000 to half within 28 minutes. When methylated inulin yields a trimethyl derivative, probably a partial hydrolysis product, and on complete hydrolysis yields 3:4:6-trimethylfructofuranose indicating that the free hydroxyls are in positions 3, 4 and 6, and the ring is a furanose type, and residues are probably united by water being eliminated from No. 1 hydroxyl of one fructose molecule with No. 2 of a second molecule. For summary see B. 1929, 1493; Bio. J. 1929, 444.

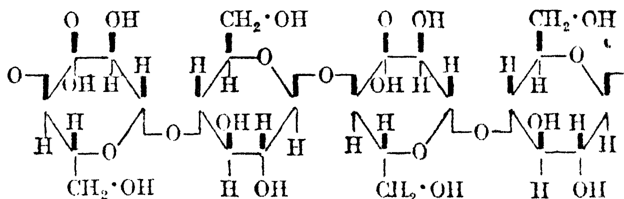


Starch and Cellulose.—On methylation starch gives an 89 per cent yield of trimethyl derivative and cellulose gives a theoretical yield of trimethylcellulose. Both products yield 2:3:6-trimethylglucopyranose on hydrolysis indicating that free hydroxyls exist in positions 2, 3 and 6 in the glucose residues in these polysaccharoses. The following formulæ have been suggested where starch contains α-glucose and cellulose β-glucose residues.

Starch with maltose residues.



Cellulose with cellobiose residues.



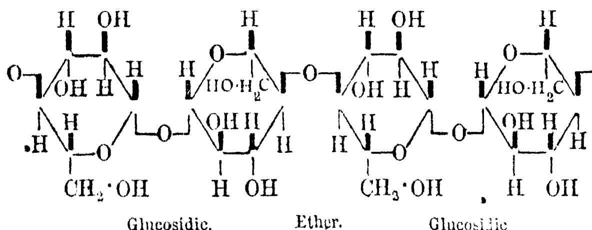
The α and β formulation respectively of starch and cellulose is supported by a comparative study of the optical rotations of their methyl and acetyl derivatives with those of the corresponding derivatives of α- and β-methylglucosides.

Such formulæ cannot, however, be regarded as accepted by all chemists. It has been suggested that the pyranose rings of hydrolysis products, such as maltose, cellobiose and trimethylglucose, are not preformed in the polysaccharoses, but are produced during the hydrolysis.

Sponsler and *Dore*,* as a result of the determination of the crystal lattice of cellulose by means of X-ray diagrams, accept the pyranose structure of the monose residues in cellulose,

* Colloid Symposium Monograph, New York, 1926.

but suggest an alternate glucosidic and ether linking, *i.e.* alternate 1:1 and 4:4 linkings of the glucose residues, *e.g.*:



Glucosidic. Ether. Glucosidic

Meyer and *Mark* (B. 1928, 593) however, do not agree with Sponsler and Dore's measurements.

In all these pyranose and furanose formulæ it must be borne in mind that in all probability the centres of the 6 or 5 atoms forming the ring do not lie in one and the same plane. The oxygen atom may lie in a plane distinct from that of the carbon atoms, or a zigzag arrangement of the atoms forming the ring may exist. This latter arrangement involves the least strain within the molecule and produces a closer packing of the atoms. But all such arrangements increases the number of stereoisomerides theoretically possible.

For recent views on the structure of the starch and cellulose molecules cf. *Haworth*, pp. 83–96.

For classification of the monosaccharoses according to their stereochemical structure and the relationships between *d* and *l* forms, see *Maltby*, J. C. S., 1923, 1404; 1926, 1629; 1929, 2769.

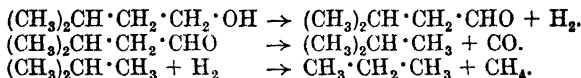
XLIX. CATALYTIC ACTION OF FINELY-DIVIDED METALS AND METALLIC OXIDES

For catalytic reductions, see Chap. XLIV, C. Finely-divided solids can act as catalysts in various other reactions.

Oxidations.—One of the most interesting of these is the dehydrogenation of primary alcohols into aldehydes and hydrogen when passed through a tube containing iron, zinc, brass, zinc oxide, ferric oxide, or stannic oxide. The method usually adopted is to use metallic copper obtained by reducing the granular fused oxide (E.P. 166, 249, 1919) and a temperature of 300°. As the reaction is endothermic the vapour of the alcohol is raised to about 300° before entering the reducing chamber. The aldehyde or ketone and unoxidized alcohol are separated by passing through fractionating columns. The gaseous products are hydrogen with 1 to 2 per cent of carbon mon- and di-oxide. With ethyl alcohol and copper at 300° practically no side reactions occur, but only 25 per cent of the alcohol used is dehydrogenated, but the 75 per cent recovered can be passed over the catalyst again and ultimately a 90-92 per cent yield of alcohol obtained. When nickel is used the side reactions, accompanied by formation of oxides of carbon, are more marked.

Iso-butyl alcohol (methyl-ethyl-carbinol) gives methyl ethyl ketone and *n*-butyl alcohol gives *n*-butaldehyde. Cyclohexanol yields cyclohexanone and borneol yields camphor, and ketonic alcohols yield diketones (Bull. Soc. 1908, [IV], **3**, 119).

The reactions: Primary alcohol $\rightleftharpoons$ aldehyde + H_2, secondary alcohol $\rightleftharpoons$ ketone + H_2, are reversible in the presence of the catalyst, as an aldehyde and hydrogen when heated in contact with zinc or iron yield an alcohol. When alcohols are heated with hydrogen under pressure, and in contact with zinc or iron, the final products consist mainly of hydrocarbons if the temperature is fairly high, *e.g.* isoamyl alcohol yields considerable amounts of propane and methane. The formation of these latter is probably due to the following series of reactions:



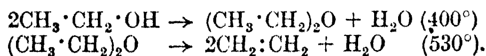
$$(CH_3)_2CH\cdot CH_2\cdot CH_2\cdot OH \rightarrow (CH_3)_2CH\cdot CH_2\cdot CHO + H_2.$$
$$(CH_3)_2CH\cdot CH_2\cdot CHO \rightarrow (CH_3)_2CH\cdot CH_3 + CO.$$
$$(CH_3)_2CH\cdot CH_3 + H_2 \rightarrow CH_3\cdot CH_2\cdot CH_3 + CH_4.$$

Reduced benzene derivatives can be oxidized to benzene

compounds, but pentamethylene derivatives are not oxidized. *Zelinsky* shows (B. **44,** 3121) that palladium black can also bring about oxidations at about 200°–300°—*e.g.* hexamethylene → benzene (ibid. p. 2302)—and gives an example, viz.: methyltetrahydro-terephthalate, which is both oxidized and reduced by hydrogen in the presence of palladium black. Glycerol in the presence of Al_2O_3 yields acraldehyde, and in the presence of finely-divided copper ethyl and alkyl alcohols (*Sabatier*, C.R. 1918, **166,** 1053).

Oxidations of hydrocarbons by air, in the presence of metallic oxides have been studied, *e.g.* for the production of formaldehyde (D. S. I. R. Chemistry Research Board Report, No. 1, 1927, and for the production of aldehydes from aromatic hydrocarbons in presence of V_2O_3 (*Walter*, 1904), Cr_2O_3 (*Loewenthal*, 1909). *Weiss* and *Downs* (J. Ind. Eng. 1920, 228; J. Ind. 1926, 188T) have shown that in oxidizing benzene the various stages are quinone, maleic anhydride and finally carbon dioxide. For the production of intermediate oxidation products the best catalysts are V_2O_3 and Mo_2O_5, and the temperature 350°–400°. As the reactions are exothermic the heat developed has to be withdrawn. Products manufactured by this process are phthalic anhydride from naphthalene; anthraquinone from anthracene, maleic anhydride from benzene. With tin vanadate as catalyst a temperature of 250°–300° suffices (*Maxted*, J. Ind. 1928, 66).

Dehydration.—When alcohols are heated at 400°–500° in the presence of aluminium oxide (Al_2O_3) a decomposition into olefine and water occurs, no aldehyde being formed. This appears to be a simple method for obtaining an olefine from the corresponding alcohol. It has been shown that the aluminium oxide loses its activity when strongly heated and rendered insoluble in acids or alkalis. Later experiments have shown that when the alcohols are heated under pressure with the oxide, the primary decomposition is into water and an ether, and that at higher temperatures the ether yields an olefine and water:

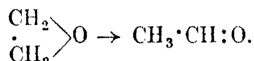


$$2CH_3\cdot CH_2\cdot OH \rightarrow (CH_3\cdot CH_2)_2O + H_2O \quad (400^\circ)$$
$$(CH_3\cdot CH_2)_2O \rightarrow 2CH_2:CH_2 + H_2O \quad (530^\circ).$$

This reaction is characteristic of primary and secondary alcohols, and does not occur in the absence of the catalyst, even when higher temperatures are used. The first reaction is

reversible, as ether, under similar conditions, yields a certain amount of alcohol.

Unsaturated hydrocarbons can also be obtained by the action of aluminium oxide on cyclic alcohols; thus menthol (p. 623) yields menthene. The same catalyst at 200°–300° is able to transform ethylene oxide and its homologues into the isomeric aldehydes:



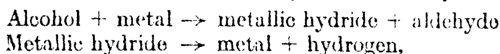
A similar change occurs in the absence of the catalyst, but at a higher temperature, viz. 500°–600°.

Numerous other substances, *e.g.* pumice, animal charcoal, sand, red phosphorus, and aluminic phosphate, can decompose alcohols into olefines and water, but oxide of aluminium appears to be the best (*Senderens*, C. R. 1907, **144**, 381, 1109). *Bouveault* has designed a special apparatus for the preparation of olefines by this method.

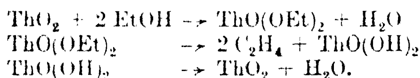
The action of silica as a catalytic agent is extremely characteristic. Pure precipitated silica, moderately calcined, decomposes ethyl alcohol at 280°, yielding pure ethylene. After it has been more strongly calcined, it induces decomposition only at a higher temperature, and then yields ethylene and water together with hydrogen and aldehyde. Pulverized quartz can yield as much as 50 per cent of the theoretical amount of hydrogen and 50 per cent of ethylene. Similarly, alumina which has been strongly calcined decomposes part of the alcohol into hydrogen and aldehyde. Experiments made with gypsum ($CaSO_4$, $2H_2O$) dehydrated below 400° and with anhydrite ($CaSO_4$) indicate that the catalytic dehydration of alcohols is effected by substances which are capable of forming temporary hydrates. Thoroughly calcined gypsum or natural anhydrite decomposes alcohol at high temperatures only, and then yields mainly hydrogen and acetaldehyde; on the other hand, gypsum which has been dehydrated at a moderate temperature is capable of combining with water, and decomposes alcohol at about 400°, yielding ethylene (*Senderens*, Annales, 1912, **25**, 449).

Sabatier and *Maihle* (Annales, 1910 [viii], **20**, 289) have studied the action of the following metallic oxides on primary alcohols, *e.g.* ethanol: ThO_2, Al_2O_3, W_2O_5, Cr_2O_3, SiO_2, TiO_2, BeO, ZrO_2, UO_2, Mo_2O_5, Fe_2O_3, V_2O_3, ZnO, MnO, CdO, Mn_3O_4, MgO. The first four act almost entirely as dehydrating agents, and at 340°–350° give 90–100 per cent yields

of olefine and little or no hydrogen (cf. *Baskerville*, J. A. C. S. 1913, **35**, 93). On the other hand, the last five oxides bring about oxidations, and give practically 100 per cent of hydrogen and no olefine. BeO and ZrO_2 give approximately equal volumes of hydrogen and olefine, *i.e.* they are mixed catalysers, as are practically all the intermediate oxides. Cf. also *Adkins*, J. A. C. S. 1922, 385, 2175; 1925, 807. According to these chemists the activity of finely-divided metals or oxides is due to the formation of unstable additive compounds; *e.g.* in catalytic oxidations of unstable hydrides:



such hydrides are readily decomposed, and yield the metal which can react with a further quantity of alcohol. With the readily reducible metals SnO, CdO, &c., a small amount of metal is formed, and this reacts as above. As the activity does not increase with time, as might be expected as more oxide becomes reduced, it is suggested that the metal gradually becomes less finely divided and hence less active. Oxides which are not readily reduced may form unstable compounds with hydrogen or with the aldehyde. The mechanism of catalytic dehydration does not consist in the formation of unstable hydrates of the catalyst as at first supposed, but in the formation of alkyl salts, *e.g.* ethyl thorate or ethyl aluminate formed by the union of the alcohol with the acidic oxide used as a catalyst:



The reaction can be utilized for obtaining iso- from *n*-butyl alcohol. The latter dehydrogenated yields Δ'-butylene, and this with sulphuric acid and subsequent hydrolysis gives the iso-alcohol, methylethylcarbinol.

Ether can be readily prepared from absolute ethyl alcohol by passing over carefully dehydrated alum at about 200° and carefully fractionating the product.

Mixed and true aromatic oxides or ethers can be readily prepared by using ThO_2 (C. R. 1914, **158**, 608). For catalytic formation of hydrocarbons cf. *Senderens* and *Murat*, Annales, 1915 [ix], **4**, 253.

Esterification.—*Sabatier* and *Maihle* (C. R. 1911, **152**, 494)

have shown that TiO_2 is a good catalyst for the conversion of acids and alcohols into esters. The method is to allow a mixture of molecular proportions of the vapour of the two compounds to pass over a column of the dioxide kept at 290°–300°. The yield of ester is about 70 per cent, and the process is extremely rapid. A similar method may be used for hydrolysing esters, *e.g.* allowing a mixture of the ester vapour with an excess of steam to pass over the dioxide at 280°–300°. Similar results are obtained with thorium oxide, provided aromatic acids are used, and glucinum oxide behaves similarly.

Formation of Amines, Nitriles, Thiols.—Amines are formed when a mixture of an alcohol and ammonia is passed over thorium dioxide at 350°–370° (C. R. 1909, **148,** 898; Bull. Soc. 1914 [iv], **15,** 327) a good yield of cyclohexylamine is obtained from the alcohol and hydrogen over nickel at 150°, and the secondary amine almost exclusively at 190° (C. R. 1929, **189**, 927); thiols (mercaptans) are formed when a mixture of alcohol and hydrogen sulphide is passed over the dioxide at 300°–360° (C. R. 1910, **150,** 1217, 1569). The yields are especially good with primary alcohols, and even phenol gives a 17-per-cent yield of thiophenol at 430°–480°; and metallic sulphides, especially CdS, at 320°–330°, decompose thiols into alkyl sulphides and hydrogen sulphide. Nitriles are formed when aliphatic acids and ammonia are passed over Al_2O_3 or ThO_2 at 500° (*Epps* and *Reid*, J. A. C. S. 1916, **38,** 2128). They are also formed when secondary and tertiary aliphatic amines are passed over nickel at 350°–380° (*Maihle*, C. R. 1917, **165,** 557; 1918, **166,** 996), hydrogen and unsaturated hydrocarbons being formed at the same time, or when esters and ammonia or aldehydes and ammonia are passed over ThO_2 at 420°–440° (ibid. 1918, **166,** 121, 215).

Ketones.—Ketones can be prepared by the action of acid anhydrides or acids on thorium dioxide at 400°. Simple and mixed aliphatic ketones and mixed aromatic aliphatic ketones have been prepared, the mixed ketones by using mixtures of two acids. Aromatic acids containing the carboxylic group attached to the benzene nucleus do not react unless mixed with an aliphatic acid, but acids of the type of phenylacetic do. The reaction probably consists in the formation of a salt and its subsequent decomposition into ketone, carbon dioxide and water. (*Senderens*, Annales, 1913, **28,** 243; *Pickard* and *Kenyon*, J. C. S. 1913, **103,** 1923.) Calcium or

barium carbonate at 450°–500° can also be used in the case of acetic acid (*Squibb*, J. A. C. S. 1895, 187). When mixed acid vapours are passed over Fe_2O_3 at 470°–480°, ketones are formed, more particularly from acids of the type of phenylacetic and cinnamic acids (*Mailhe*, Bull. Soc. 1914, **15**, 324). Manganous oxide, MnO, also gives good results, *e.g.* 70 per cent yields. By this process adipic acid gives cyclopentanone (C. R. 1914, **158**, 830, 985). This oxide is of use for the preparation of acetone, as even dilute (20 per cent) solutions of acetic acid passed over MnO at 350° give theoretical yields of acetone (*Sidgwick* and *Lambert*, 1915).

A mixture of an acid with an excess of formic acid passed over TiO_2 at 250°–300° yields the aldehyde, with the exception of acids of the benzoic type, and even better results are obtained with MnO (*Sabatier* and *Mailhe*, C. R. 1912, **154**, 561; 1914, **158**, 985).

Formic acid behaves somewhat differently from the other fatty acids (*Sabatier* and *Mailhe*, C. R. 1911, **152**, 1212). Finely-divided Pd, Pt, Ni, Cu, Cd, and ZnO or SnO decompose it into carbon dioxide and hydrogen. TiO_2 and W_2O_5 yield water and carbon monoxide, and SiO_2, ZrO_2, Al_2O_3, &c., give both reactions.

A study of the synthetical value of acetylene in the presence of finely-divided metallic oxides has been made by *Tschitschibabin* (J. Russ. 1915, **47**, 703). Acetylene and ammonia over heated Al_2O_3, Fe_2O_3, or Cr_2O_3 at 300° yield pyridine bases, mainly α- and γ-picolines (p. 572) and 2-methyl-3-ethylpyridine, together with pyrrole and piperidine bases. Acetylene and hydrogen sulphide over Al_2O_3 give thiophene, and the method is recommended as a commercial one. Similarly acetylene and water over Al_2O_3 at 400°–425° yield furane.

Iodine.—The use of small amounts of iodine as a catalyst in the chlorination of acetic acid or the bromination of benzene (p. 384) has long been recognized. *Knoevenagel* (J. pr. 1914, **89**, 1) finds that small amounts of iodine accelerate many reactions and lead to the formation of purer products. This is especially noticeable in (*a*) the formation of thiodiarylamines from sulphur and diarylamine, the presence of 0·05 to 0·2 per cent of iodine producing a marked effect; (*b*) the condensation of aromatic amines with naphthols or naphthylamines; (*c*) the alkylation of primary aromatic amines, especially aniline and α-naphthylamine, by the direct action of alcohols; (*d*) the condensation of aromatic alcohols with ketones. Minute

quantities of iodine are of value in obtaining unsaturated compounds by heating hydroxy compounds, *e.g.* unsaturated hydrocarbons from alcohols, unsaturated ketones from ketonic alcohols, and unsaturated aldehydes from aldols. The reagent is also of value in condensing glycols to polyglycols (*Hibbert*, J. A. C. S. 1915, **37**, 1748), or in reactions involving elimination of hydrogen chloride (*Desai*, J. I. I. S. 1924, 235).

Aluminium chloride.—In the *Friedel-Crafts* reaction (pp. 374, 457) for the synthesis of aromatic hydrocarbons, ketones and di- and triphenyl-methane derivatives, aluminium chloride or an analogous metallic chloride is used as the condensing or catalytic agent. The amount of metallic chloride required varies considerably with the constitution of the reacting acid chloride and hydrocarbon. In some cases traces are sufficient, in others a molecular proportion or more is essential, in order to obtain good yields. Aluminium chloride and analogous chlorides form well-defined additive compounds, not only with acyl chlorides but also with numerous other organic compounds (*Menschutkin*, Abs. 1909, i, 897; 1911, i, 273, 532; 1912, i, 100; ii, 922; *Perrier*, B. 1900, **33**, 815), and it is possible that the additive compounds are the reactive reagents (*Boeseken*, Abs. 1910, i, 152; 1911, i, 173), but often the reactive acyl or akyl halogen compounds are not those which readily yield additive compounds with metallic chlorides, and the effect of the latter appears to be to produce a loosening of the halogen in the organic compound (Rec. trav. 1913, **32**, 1).

The dynamics of the reaction have been investigated. In the benzoylation of anisole in the presence of $SnCl_4$ or $AlCl_3$ the velocity is proportional to the concentration of the catalyst (Zeit. phys. 1904, **48**, 424).

By a study of the reaction between *p*-bromobenzene-sulphonyl chloride and benzene in the presence of $AlCl_3$, *Olivier* (Rec. trav. 1914, **33**, 91) draws the following conclusions:—(1) The acyl chloride reacts solely in the form of the additive compound with $AlCl_3$. (2) One molecule of $AlCl_3$ cannot transform more than one molecule of the acyl chloride. (3) The reaction is unimolecular with respect to the additive compound. (4) In the absence of excess of $AlCl_3$ the velocity constant is proportional to the concentration of the $AlCl_3$, when K is calculated for the compound $C_6H_4Br \cdot SO_2Cl, AlCl_3$. (5) The velocity is greatly increased by an excess of $AlCl_3$. These facts point to the conclusion that the acyl chloride is

activated proportionally to the concentration of the combined $AlCl_3$ (cf. *Rubidge* and *Qua*, J. A. C. S. 1914, **36**, 732).

Boeseken and others (Abs. 1913, ii, 575; 1914, i, 156) consider that the aluminium chloride also activates the aromatic hydrocarbon by disturbing its residual affinity.

In certain cases the acyl chloride may form an additive compound with the hydrocarbon, *e.g.* hexene yields 2-chlorocyclohexyl methyl ketone and this by loss of HCl gives tetrahydroacetophenone (*Wieland* and *Bettag*, B. 1922, 2246).

When antimony chloride is used an additive compound with the hydrocarbon is first formed, *e.g.* $2SbCl_3, C_6H_5R$, which then reacts with the acyl chloride, *e.g.* benzoyl chloride, yielding an additive compound of the ketone and antimony chloride, which decomposes into its constituents at the temperature of the experiment; and the liberated $SbCl_3$ can then react with fresh quantities of hydrocarbon (*Menschutkin*, Abs. 1914, i, 188, 673).

Senderens (J. Ind. 1927, 681, 702) holds the view that in *all* cases there is definite, if unstable, compound formation between one of the substances used and the catalyst. This may be formed in only small amount, and may be of the type of a hydride NiH_2, an oxide Cu_2O, Ag_2O, a salt as in acetone formation or an ester as in formation of olefines, amines, thiols, &c. The alcohol used forms an alkyl thorate (or aluminate) and this can form an ether or an olefine or can react with ammonia to form amines, or with hydrogen sulphide to form thiols. Attention is drawn to the reversibility of many of the reactions, and the inverse reaction is often favoured by a rise of temperature, *e.g.* $CH_3{\cdot}CH_2{\cdot}OH \rightleftharpoons CH_3{\cdot}CH{:}O + 2H$.

The "intermediate compound" theory of heterogeneous catalysis has practically replaced the theory of adsorption and formation of abnormally concentrated layers on the surface of the catalyst, with the result that chemical action was accelerated without the catalyst taking any chemical part in the change (*van 't Hoff*). This physical view fails to account for the different behaviour of the same chemical compound under the influence of two different catalysts, *e.g.* alcohol with copper at 300° gives aldehyde and hydrogen, but with alumina gives ethylene and water, or formic acid with zinc oxide gives CO_2 and H_2, but with titania yields CO and H_2O. It also fails to account for such changes as that of oleic into isoleic acid during hydrogenation. According to *Langmuir* (J. A. C. S. 1916, 2221; 1917, 1848; 1918, 1361) the primary condition of

adsorption of a gas at a solid surface is due to a single layer of molecules which are held at the surface by a force which is indistinguishable in effect from chemical affinity. The physical view thus approximates to the "intermediate compound" theory. Although intermediate compounds may be formed in many cases it is impossible actually to isolate them, they are only a stage in the chemical change. Thus *Armstrong* and *Hilditch* (P. R. S. A. 1919, **96**, 137; 1920, **98**, 27) in cases of hydrogenation of unsaturated compounds consider that both the unsaturated compound and the hydrogen form labile compounds with the nickel.

With any given catalyst the nature of the surface plays a most important part, thus with a metallic oxide the temperature at which it is formed may be a deciding factor as to its activity or non-activity; similarly with a metal its state of division, the temperature to which it has been subjected, and whether spread over a large surface, *e.g.* nickel or Kieselgühr or a compact powder. *Taylor* (P. R. S. A. 1925, **108**, 105; J. Ph. Chem. 1926, 150) claims that many of the phenomena are in harmony with the view that in an active catalyst although the general structure is that of a crystal lattice, the surface is irregular, and has local excrescences of atoms, *i.e.* atoms thrust irregularly at various points above the normal surface of the metal (in the case of nickel). Such atoms more or less separated from its fellows may be more "unsaturated" and more prone to enter into chemical action.

Characteristic of catalytic processes as solid surfaces is the readiness with which the catalyst may become "poisoned" or rendered inactive, *e.g.* nickel in cases of hydrogenation by traces of sulphur compounds, of carbon monoxide or of colloidal matter. All primarily due to the adsorption of the poison on the surface and then either simply covering the active nuclei with a protective layer and preventing the hydrogen and liquid or vapour coming into contact with the catalyst or actually destroying the chemical nature of the surface, *e.g.* conversion into sulphide. A useful partial poisoning effect is observed in the case of palladium supported on barium sulphate (cf. p. 186). Without the support palladium will bring about the reduction of an acid chloride to benzyl alcohol, but in the presence of the barium sulphate it is slowed down and good yields of benzaldehyde can be obtained. For general discussion cf. *Hilditsch*, Catalytic Processes, p. 15.

L. UNSATURATION

A. Types of Unsaturation

The term unsaturated has been frequently applied in earlier chapters to different compounds without any clear definition of the term. It has been used to comprise all cases of compounds which are capable of uniting with other elements or compounds, thus olefines with bromine or hydrogen, aldehydes with hydrogen cyanide or bisulphites. The best definition is "Unsaturated compounds are those capable of uniting with another substance (element or compound) without a disruption of their original structure." Two main types may be distinguished.

I. Cases in which the addenda unite with one and the same atom of the original compound, as in the conversion of amines into salts and quaternary ammonium compounds, the formation of oxonium salts from ethers, &c., and the formation of sulphonium salts from alkyl sulphides.

The presence of such unsaturated groups as amino and hydroxyl, and also the alkylated groups, ·NHR, $\cdot NR_2$, ·OR, produce marked effects on the properties of the compounds into which they are introduced. In the aromatic series they render the compounds much more reactive towards reducing, oxidizing, and substituting reagents (cf. p. 438). When further substituents are introduced, *e.g.* Cl, Br, SO_3H, NO_2, &c., these almost invariably take the ortho and para positions with respect to the unsaturated group. These groups also tend to make the compound luminesce under the influence of electric discharges under small pressures. They are also the most powerful *auxochromes* known; *i.e.* when introduced into a compound containing chromophores, such as, ·N:N, C:O, C:C, NO_2, &c., they produce a deepening of the colour of the compound.

In each case the atom involved passes to a higher valency state, *e.g.* from 2 to 4 or 3 to 5, and in practically all cases the product formed is an ionizable salt, *i.e.* the element in question with its attached groups acts as a cation.

Salt Formation in Case of Cyclic Oxygen Compounds.—This has been studied in the case of pyrones and similar compounds (*B. W. Ghosh*, J. C. S. 1915, **107**, 1588) by means

of perchloric acid. Many ring compounds containing one or two atoms of oxygen do not form oxonium salts with perchloric acid, *e.g.* $O\langle{}^{CH_2\cdot CH_2}_{CH_2\cdot CH_2}\rangle CH_2$, $O\langle{}^{CH_2\cdot CH_2}_{CH_2\cdot CH_2}\rangle O$, and the corresponding compounds condensed with a benzene nucleus. The introduction of olefine linkings, the replacement of CH_2 by CO, or an accumulation of benzene nuclei increase the basic properties of the oxygen and facilitate salt formation.

An attempt to settle the structure of salts of simple unsymmetrical γ-pyrones has been made by *Gibson* and *Simonsen* (J. C. S. 1928, 2307) by trying to isolate two 2-methyl-6-phenyl-4-pyrone *d*-α-bromocamphor-sulphonates, no isomerides could be detected, and they consider this favours the *pyrylium* structure I rather than the ordinary oxonium formula II.



The pyrylium structure is met with in many anthocyanidins.

Molecular Compounds.—Analogous to the unstable oxonium salts are the additive compounds formed by the union of aromatic compounds, more particularly amines, phenols, and phenolic ethers with quinones and aromatic nitro-compounds of the type of *s*-trinitrobenzene, polynitronaphthalenes, and even *m*-dinitrobenzene. Many of these compounds are highly coloured, and since the more complex aromatic hydrocarbons also combine with quinones and nitro derivatives, it is highly probable that the union is the result of the neutralization of the residual valency of the aromatic nuclei by that of the nitro groups. (J. C. S. 1916, 1339; A. 1914, **404**, ii; 1916, **412,** 253; 1924, **440**, 265; *Pfeiffer*, "Organische Molekülverbindungen", 2nd Edition, 1927; *Bennett* and *Willis*, J. C. S. 1929, 256, who give electronic formulæ for such compounds.)

II. The addenda become attached to two different atoms, which may be (*a*) adjacent atoms, (*b*) atoms removed from one another by a chain of one or more atoms. Type (*b*) is not very common, and the best known example is the addition of bromine to cyclopropane accompanied by the breaking of the tri-ring and the formation of the open-chain compound, trimethylene bromide, $CH_2Br\cdot CH_2\cdot CH_2Br$.

The common type is (*a*) *e.g.* the addition of 2H to ethylene to form ethane, or of bromine to oleic acid to form 8:9-dibromostearic acid.

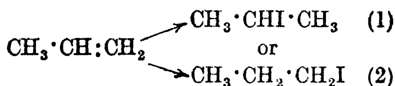
It has been definitely proved in the case of ethylene dibromide that the bromine atoms are attached to different carbon atoms (p. 65) and somewhat similar arguments can be used in other cases.

Compounds of type (*a*) are usually represented as containing double or triple linking between the two adjacent atoms, *e.g.* C:C, C:N, C:O, C:S, S:O, N:N, C:C, C:N, &c. This merely means that all the valencies which are not used up in attaching H or other element or group to C, O, S, or N, are used up in attaching C to C, C to O, C to N, &c. In terms of the electronic conception of valency this means that with a double linkage between C and C, C and O, and C and N, N and N, each of the two atoms shares 4 electrons, two coming from each of the two atoms concerned, so that each atom retains its electrical neutrality. In certain cases of S and O and N and O, the double linkage is of a different type, viz. a semipolar linkage, cf. Chap. XLVII under Parachor.

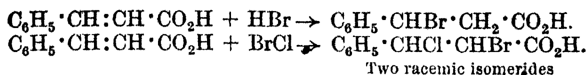
In examples of the first type the question as to whether addition or not takes place depends upon a variety of factors. (1) Whether the double linking is between C and C, C and O, C and N, or N and N. Thus although both olefines and carbonyl derivatives combine with hydrogen, the first group adds on bromine readily, whereas the second does not; and the second combines with hydrogen cyanide or sodium bisulphite more readily than the first group does. (2) The nature of the groups already attached to the two atoms which are united by the double linking. Thus although most olefine derivatives combine with bromine, compounds in which there are several negative groups, such as Ph, Br, CN, CO_2H, already attached to the two carbon atoms, do not form additive compounds with bromine (*Hugo* and *Bauer*, B. **37**, 3317; *H. Ley*, B. 1917, **50**, 243), although they contain an olefine linking. They combine, however, with chlorine (*Behr*, B. 1910, 2940; *Meisenheimer*, A. 1927, **456**, 142.) On the other hand, olefine compounds, containing two methyl groups attached to one of the two ethylene carbon atoms do not readily combine with hydrogen, but form additive compounds with bromine, *e.g.* dimethyl-cinnamene, CHPh:CMe_2 or terpinolene (p. 620). (3) The nature of the addenda. It has been pointed out already (p. 46) that chlorine combines most readily and iodine least readily, but that hydrogen iodide combines more readily than hydrogen chloride or bromide. (4) Conditions of the experi-

ment, *e.g.* nature of solvent, sunlight, temperature, presence of a catalyst, &c. Phenyl-propiolic acid does not combine with hydrogen chloride when in aqueous solution below 80°.

When the two addenda are the same it is immaterial whether the original compound involved has a symmetrical or unsymmetrical structure, thus the symmetrical ethylene can yield only one dibromide and similarly the unsymmetrical propylene, $CH_3 \cdot CH:CH_2$, can yield only a single dibromide. With a symmetrical compound only one product can be formed, even when the addenda are different, thus ethylene can yield only the one ethyl iodide. The matter is not so simple when two different addenda unite with the two C atoms of an unsymmetrical olefine; thus propylene and hydrogen iodide can give theoretically two distinct additive compounds.



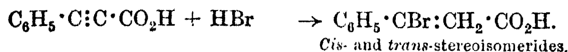
In practice the first reaction proceeds almost to the exclusion of the second, according to *Michael* the proportions of (1) and (2) formed are practically in the ratio of 300:1. It can be stated as a general rule that, in the addition of halogen hydracid to an olefine linking, the halogen unites with the carbon atom which has the lesser number of hydrogen atoms attached to it. If the two addenda are chemically not so different as H and I, *e.g.* I and Cl, then the two products formed are in the proportion $CH_3 \cdot CHCl \cdot CH_2I$ and $CH_3 \cdot CHI \cdot CH_2Cl$ as 3 is to 1, and with Br and Cl the proportions of $CH_3 \cdot CHCl \cdot CH_2Br$ and $CH_3 \cdot CHBr \cdot CH_2Cl$ as 1·4:1. In all cases the more negative of the two atoms tends to unite with the CH rather than the CH_2 group. *Michael* has attempted to collate all such phenomena under his " Distribution Principle " (J. pr. 1888, [ii], **37**, 524; 1899, **60**, 286, 409; 1903, **68**, 487; B. 1906, 2138). According to this the two interacting molecules combine in the manner which produces the most chemically saturated compound, and this neutralization of affinities depends not only on the chemical characteristics of the addenda, but also on the character of the atoms to which the addenda become attached. Other interesting cases are the addition of HBr and BrCl to cinnamic and phenylpropiolic acids (*Hanson* and *James*, J. C. S. 1928, 1955, 2979)—



$$C_6H_5\cdot CH:CH\cdot CO_2H + HBr \rightarrow C_6H_5\cdot CHBr\cdot CH_2\cdot CO_2H.$$

$$C_6H_5\cdot CH:CH\cdot CO_2H + BrCl \rightarrow C_6H_5\cdot CHCl\cdot CHBr\cdot CO_2H.$$

Two racemic isomerides



$$C_6H_5\cdot C⋮C\cdot CO_2H + HBr \rightarrow C_6H_5\cdot CBr:CH_2\cdot CO_2H.$$

Cis- and *trans*-stereoisomerides.



$$C_6H_5\cdot C⋮C\cdot CO_2H + BrCl \rightarrow C_6H_5\cdot CCl:CBr\cdot CO_2H.$$

Cis- and *trans*-stereoisomerides.

In all these cases the less negative of the two addenda (H in HBr and Br in BrCl) combines with the β-carbon atom and not with the C atom to which the carboxyl group is directly attached.

All such phænomena may find an explanation in the electronic structure of atoms.

In addition to the additive reactions discussed in the preceding chapters there are several others of considerable interest. One of these is the addition of alkali metals to double linkings (*Schlenk* and others, B. 1914, **47**, 473). In ethereal solution many compounds containing the groupings C:C, C:N, N:N, combine with sodium, and the structure of the additive compounds is deduced from a study of the products formed by the action of water or carbon dioxide. Thus the sodium derivative of stilbene, CHPh:CHPh, yields *s*-diphenylethane with water and *s*-diphenyl-succinic acid with carbon dioxide. In a similar manner the acid, $CO_2H\cdot NPh\cdot NPh\cdot CO_2H$, can be prepared from azobenzene.

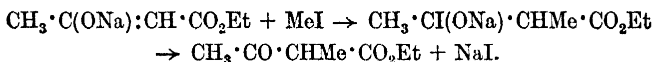
This additive reaction is by no means general for unsaturated compounds. With olefine compounds only those react with sodium which contain benzene nuclei attached to both atoms of carbon, *e.g.* stilbene and anthracene, the latter giving rise to the compound $C_6H_4\langle{}^{CHNa}_{CHNa}\rangle C_6H_4$. In the case of 1:1-diphenylethylene, $CPh_2:CH_2$, only the CPh_2 takes up Na, so that the product is $Na\cdot CPh_2\cdot CH_2\cdot CH_2\cdot CPh_2\cdot Na$. With the C:N linking addition to both atoms occurs when two benzene nuclei are attached to the C atom, *e.g.* benzophenoneanil, $CPh_2:NPh$, yields $Na\cdot CPh_2\cdot NPh\cdot Na$, whereas benzaldehydeanil CHPh:NPh yields $Na\cdot NPh\cdot CHPh\cdot CHPh\cdot NPh\cdot Na$.

Compounds with sodium attached to two adjacent atoms behave abnormally, with alkyl halides they yield the original unsaturated compound, and a dialkyl, *e.g.* $CH_3\cdot CH_3$ or $C_2H_5\cdot C_2H_5$; but when the sodium atoms are in positions 1:4

the reaction is normal and the sodium atoms become replaced by alkyl groups.

Ethyl diazoacetate also combines with certain olefines (cf. p. 630) and results in the elimination of nitrogen and the formation of an ester derived from cyclopropane.

It is highly probable that the reaction between alkyl halides or acyl chlorides and the sodium derivative of ethyl acetoacetate is of an additive character (pp. 236–237) (*Michael*, J. pr. 1899, **60**, 295; *Nef*, A. 1899, **266**, 52; 1893, **276**, 235; 1894, 280, 314).



$$CH_3 \cdot C(ONa){:}CH \cdot CO_2Et + MeI \rightarrow CH_3 \cdot CI(ONa) \cdot CHMe \cdot CO_2Et$$
$$\rightarrow CH_3 \cdot CO \cdot CHMe \cdot CO_2Et + NaI.$$

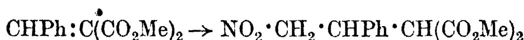
In a similar manner the condensation of the esters of unsaturated esters with the sodium derivative of ethyl malonate, ethylacetoacetate, or ethyl cyanoacetate is also additive (*Michael's* reaction). The unsaturated compound should contain a positive group attached to one ethylenoid C atom, and a strongly negative group, *e.g.* CO_2H, CN, to the other. Then the sodium always adds on to the latter carbon atom, and the $CH(CO_2Et)_2$ or $CH_3 \cdot CO \cdot CH(CO_2Et)$ to the former. The esters of fumaric, maleic, aconitic, crotonic, citraconic, itaconic, acetylenedicarboxylic, and phenylpropiolic acids and benzylideneacetone, all react in a similar manner but at different rates (*Auwers*, B. 1895, **28**, 1131; A. 1896, 292, 147). The reaction is of considerable value for synthesizing polybasic acids, *e.g.* 2-phenylpropane-1:1:3-tricarboxylic acid can be obtained from ethyl cinnamate and ethyl sodiomalonate, and from benzylidene-acetone and ethyl sodiomalonate the additive compound, $C_6H_5 \cdot CH \langle \begin{array}{l} CH(CO_2Et)CO_2Et \\ CH_2 \cdot CO \cdot CH_3 \end{array}$, which readily loses alcohol, giving $C_6H_5 \cdot CH \langle \begin{array}{l} CH(CO_2Et) \cdot CO \\ CH_2 \text{———} CO \end{array} \rangle CH_2$, ethyl phenyldihydroresorcilate. A modification of the reaction consists of using the free malonic, aceto-acetic, or cyano-acetic ester in the presence of a little diethylamine (*Knoevenagel*, B. 1904, **37**, 4464). The sodium salts of the unsaturated acids can sometimes be used instead of the esters (*Reinicke*, A. 1905, **341**, 80).

The *Michael* reaction is a balanced one, so that as a rule

yields are not quantitative, but can be improved by removing the condensation product and continuing the reaction.

Hydrogen cyanide, sodium bisulphite, and other compounds can react with olefine compound containing a C:O union in conjugation, *e.g.* benzylidene-malonic ester, $C_6H_5 \cdot CH:C(CO_2Et)_2$ and HCN give $C_6H_5 \cdot CH(CN) \cdot CH(CO_2Et)_2$ (*Lapworth*, J. C. S. 1903, 995; 1904, 1206; 1906, 945).

Nitromethane combines with olefine compounds. With unsaturated esters addition takes place in dry methyl alcohol containing sodium methoxide. H adds on to the C atom to which the CO_2Et group is attached, and $\cdot CH_2 \cdot NO_2$ to the adjacent C atom; thus the methyl ester of benzylidene-malonic acid:


$$CHPh:C(CO_2Me)_2 \rightarrow NO_2 \cdot CH_2 \cdot CHPh \cdot CH(CO_2Me)_2$$

with an unsaturated ketone, *e.g.* phenyl styryl ketone:


$$CHPh:CH \cdot CO \cdot Ph \rightarrow NO_2 \cdot CH_2 \cdot CHPh \cdot CH_2 \cdot COPh.$$

(*Kohler*, J. A. C. S. 1916, **38**, 889; 1919, **41**, 764.)

Addition to the carbonyl of hydrogen, hydrogen cyanide, alcohol, sodium bisulphite, Grignard reagents, &c., has already been discussed under aldehydes and ketones. Different carbonyl compounds react at very different rates, and the following is the order of relative reactivity:


$$\cdot CO \cdot CH_3, \ \cdot CO \cdot C:C, \ \cdot CO \cdot OR, \ \cdot CO \cdot NH_2, \ \cdot CO \cdot OH.$$

Compare also *Goldschmidt*, B. 1896, **29**, 105.

In the case of a series of ketones the introducton of negative groups, *e.g.* CO_2Et, increases the reactivity of a ketone, whereas alkyl groups lessen the reactivity of the CO group towards sodium bisulphite (*Stewart*, J. C. S. 1905, **87**, 186; *Petrenko-Kritschenko*, A. 1905, **341**, 150). For additions to $\alpha:\beta$ unsaturated ketones cf. *Vorländer*, ibid. p. 9.

Colour Test for Unsaturation.—Tetranitromethane (p. 100) has been used as a reagent for testing for unsaturation. All olefine compounds, with the exception of a few unsaturated acids, give a yellow coloration with the reagent, as do most aromatic compounds with the exception of nitro derivatives. Substances containing bivalent sulphur or tervalent nitrogen also give colorations, and generally there appears to be a relationship between the amount of residual affinity and

the depth of colour. A conclusion which has been confirmed by a study of the absorption spectra of tetranitromethane, or alkyl nitrites with various heterocyclic compounds containing O, S, or N in the nucleus.

Degree of Unsaturation (Hydrogen Value).—The volume of hydrogen absorbed by shaking the compound and hydrogen in the presence of molecular platinum (*Fokin*, cf. p. 680), affords a method of determining the number of olefine or acetylene linkings in a compound, but will not give the total unsaturation, e.g. C:N, N:N, C:O, &c.

The method of determining the so-called iodine value of oils used in the technical examination of fixed oils, viz. by determining the amount of Br_2 or ICl added to the oil, gives a measure of the amount of olein and more highly unsaturated glycerides present in the oil, but is useless for the estimation of such unsaturated compounds as the esters of $\alpha\beta$-unsaturated acids.

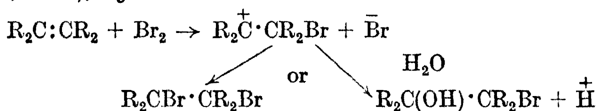
It is highly probable that many reactions which are regarded as simple substitutions are preceded by the formation of additive compounds, the so-called Kekulé molecule; cf. *Vorländer*, A. 1903, **341**, 1; 1906, **345**, 155.

B. Properties of Unsaturated Acids as affected by the position of the Double Bond

Acids which contain a double bond in the $\alpha\beta$ position differ in many respects from isomeric acids in which this bond is further removed from the carboxylic group.

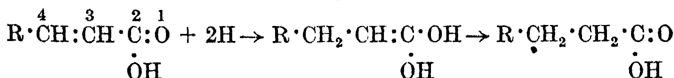
The $\alpha\beta$ unsaturated acids are reduced much more readily than their isomerides by sodium amalgam and water. This is somewhat remarkable, since in the case of other additive reactions, for example, the addition of bromine, the $\alpha\beta$ unsaturated acids are usually less reactive, *i.e.* do not combine with bromine in chloroform or carbon tetrachloride solutions so readily as $\beta\gamma$ unsaturated acids or other acids in which the double bond is far removed from the carboxyl group (*Sudborough* and *Thomas*, J. C. S. 1910, 715, 2450; *Williams* and *James*, 1928, 343; *Ponzio* and *Gastaldi*, G. 1912, **42**, ii, 92. The rate of addition of bromine to a cinnamic acid is greatly increased by the presence of an *ortho* or *para* methoxy group, and probably by ortho or para NR_2 groups (J. C. S. 1928, 344; J. I. I. S. 1925, 193). The reaction is not a simple bimolecular

reaction in carbon tetrachloride solution, probably substitution occurs liberating a small amount of hydrogen bromide which acts as a catalyst and thus the values of k increase with the time. Certain conjugate compounds with one olefine linking in the $\alpha\beta$ position to the carboxylic group, *e.g.* cinnamylidene-acetic acid combine with bromine fairly readily. The composition of a mixture of $\alpha\beta$ and $\beta\gamma$ isomeric acids has been determined by *Linstead* (J. C. S. 1927, 356) by comparing the velocity of addition of the mixture with the velocities of the two pure acids. The addition of BrCl is much more rapid than that of Br_2 or even Cl_2. In substitution and additive reactions with bromine it appears to be the molecule and not separate ions which first comes into play (*Soper* and *Smith*, J. C. S. 1926, 1582), as soon as one Br atom (or ion) is fixed the other ion is liberated and is free to be fixed (*Francis*, J. A. C. S. 1925, 2340), *e.g.*:



The latter reaction with water accounts for the formation of an additive product with OH and Br (or OH and Cl) in aqueous solution, and thus renders unnecessary the supposition that hypobromous acid HBrO is the addendum. It is highly improbable that HBrO would add on in the manner given. Similarly the conversion of cinnamic acid into α-chloro-β-ethoxy-β-phenylpropionic acid, $OEt\cdot CHPh\cdot CHCl\cdot CO_2H$, by chlorine in alcoholic solution can be accounted for by the primary formation of $\overset{+}{C}HPh\cdot CHCl\cdot CO_2H$, and the reaction of this with ethyl alcohol yielding the β-ethoxy compound (J. A. C. S. 1927, 2071).

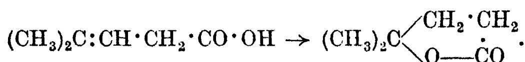
The readiness with which $\alpha\beta$ unsaturated acids can be reduced may perhaps be accounted for by the presence of the conjugated double bonds (cf. p. 840)—



1:4 addition takes place, but the resulting unsaturated glycol is unstable and, by a wandering of an atom of hydrogen, yields the saturated acid.

J. Bougault (C. R. 1905, i. 9; cf. *Linstead* and *May*, J. C. S. 1927, 2566) shows that $\beta\gamma$ unsaturated acids combine with the elements of hypoiodous acid (HIO), yielding lactones, whereas the isomeric $\alpha\beta$ acids do not. This provides the basis of a method for separating a mixture of an $\alpha\beta$ and $\beta\gamma$ unsaturated acid.

One of the best methods of separating a mixture of $\alpha\beta$ and $\beta\gamma$ unsaturated acids is due to *Fittig* (B. 1894, **27**, 2667; A. 1894, **283**, 51), and consists in heating the acids for a few minutes at 140° with a mixture of equal volumes of concentrated sulphuric acid and water. The $\alpha\beta$ acid is unaffected by this treatment, whereas the $\beta\gamma$ acid is converted into a γ-lactone (p. 225) which is insoluble in sodium carbonate solution.



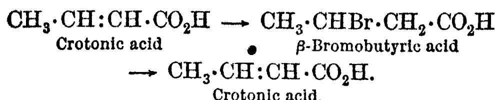
When this method is used, only the $\alpha\beta$ acid can be recovered. A method by means of which both acids can be recovered is the separation by fractional esterification, as an $\alpha\beta$ acid is esterified much less readily than iosmeric unsaturated acids (*Sudborough* and *Thomas*, J. C. S. 1911, 2307; *Eccott* and *Linstead*, 1929, 2153).

One of the best methods for determining the position of the double bond in the case of an olefine acid is by an examination of the oxidation products (p. 168). These consist, as a rule, of a mixture of a monobasic and a dibasic acid, as the carbon atoms between which the olefine bond functionated both yield carboxylic groups; *e.g.* $R{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CO_2H$ gives $R{\cdot}CO_2H$ and $CO_2H{\cdot}CH_2{\cdot}CO_2H$. Cf. also Oleic acid, p. 171.

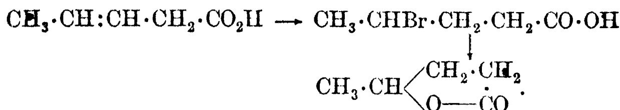
Dimethylacrylic acid $(CH_3)_2C{:}CH{\cdot}CO_2H$, when oxidized yields acetone, $(CH_3)_2CO$, and oxalic acid or, its oxidation product, carbonic acid.

The conversion into ozonides and the decomposition of these (p. 694) is also used for the determination of the position of the double linking.

Another method adopted for determining the position of an olefine bond is by an examination of the hydrobromide. If the bond is in the $\alpha\beta$ position the bromo-derivative of the saturated acid loses hydrogen bromide when treated with alkali and yields the original olefine acid.


$$CH_3\cdot CH:CH\cdot CO_2H \rightarrow CH_3\cdot CHBr\cdot CH_2\cdot CO_2H \rightarrow CH_3\cdot CH:CH\cdot CO_2H.$$
Crotonic acid — β-Bromobutyric acid — Crotonic acid.

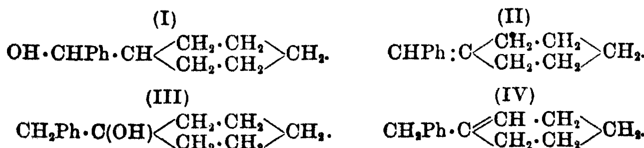
A βγ or γδ unsaturated acid also yields a hydrobromide, but when this is treated with alkalis hydrogen bromide is eliminated and a lactone formed.


$$CH_3\cdot CH:CH\cdot CH_2\cdot CO_2H \rightarrow CH_3\cdot CHBr\cdot CH_2\cdot CH_2\cdot CO\cdot OH \rightarrow CH_3\cdot CH<\begin{matrix}CH_2\cdot CH_2\\ O\text{---}CO\end{matrix}.$$

The presence of olefine linkings, as in maleic anhydride, increases to an appreciable extent the readiness with which the anhydride combines with water (*Ribett* and *Sidgwick*, J. C. S. 1910, 1677).

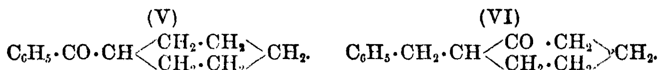
An extremely simple method of determining whether the double bond is in the αβ position or not, is by an examination of the rate of esterification of the unsaturated acid and of its saturated analogue by the catalytic method. An αβ acid is esterified much more slowly than its saturated analogue, the βγ-isomeride somewhat more readily than the saturated acid, and acids in which the double bond is still further removed from the carboxyl group have much the same esterification constants as the corresponding saturated acids (*Sudborough* and *Gittins*).

A method for determining the position of the olefine linking in the case of an unsaturated cyclic hydrocarbon has been worked out by *Auwers* and *Treppmann* (B. 1915, **48**, 1207, 1377). The hydrocarbon formed by the elimination of water from phenylcyclohexyl carbinol (I) should have the structure represented by (II), but as it is also formed by eliminating water from 1-benzylcyclohexan-1-ol (III) it may have the structure (IV):


(I) $OH\cdot CHPh\cdot CH<\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot CH_2\end{matrix}>CH_2.$ (II) $CHPh:C<\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot CH_2\end{matrix}>CH_2.$

(III) $CH_2Ph\cdot C(OH)<\begin{matrix}CH_2\cdot CH_2\\ CH_2\cdot CH_2\end{matrix}>CH_2.$ (IV) $CH_2Ph\cdot C\lessdot\begin{matrix}CH\cdot CH_2\\ CH_2\cdot CH_2\end{matrix}>CH_2.$

By the addition of nitrosyl chloride the Cl attaches itself to the tertiary carbon atom and the NO to the CH group, which becomes transformed into $\cdot C:N\cdot OH$ group, and this on hydrolysis to CO; the final products would therefore be either benzoylcyclohexane (V) from (II), or 1-benzylcyclohexan-2-one (VI) from (IV):



The actual product isolated was not the known benzoylcyclohexane, and hence was presumably 1-benzyl-cyclohexan-2-one and the original hydrocarbon 1-benzyl-Δ^1cyclohexene (II).

For the stereochemistry of compounds containing only one ethylene linking, cf. p. 251. When two or more olefine bonds are present in the molecule, the isomerism is more complex. Not merely can we have structural isomerides, which differ in the relative positions of the olefine linkings, but also the number of stereoisomerides increases.

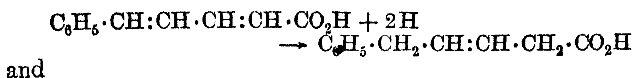
For compounds of type, Cab:C:Cab, see p. 703.

C. Compounds with Conjugate Double Bonds

One of the most interesting groups containing two double linkings comprises the compounds with conjugate double bonds. Within recent years numerous experiments have been made with compounds containing two double bonds in the relative positions indicated by the formula—

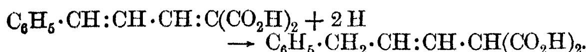


These have been termed conjugated double bonds by *Thiele*, and extremely interesting results have been obtained by the study of the additive reactions of such compounds. It is found that the atoms or radicals added on do not, as a rule, become attached to the carbon atoms 1 and 2 or 3 and 4, but to numbers 1 and 4; so that a new ethylene linkage is created in position 2:3. Thus cinnamylideneacetic and cinnamylidenemalonic acids when reduced yield 1:4-dihydro-derivatives (*Rüber*, B. 1904, **37**, 3120)—



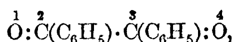
$$C_6H_5\cdot CH:CH\cdot CH:CH\cdot CO_2H + 2H \rightarrow C_6H_5\cdot CH_2\cdot CH:CH\cdot CH_2\cdot CO_2H$$

and



$$C_6H_5\cdot CH:CH\cdot CH:C(CO_2H)_2 + 2H \rightarrow C_6H_5\cdot CH_2\cdot CH:CH\cdot CH(CO_2H)_2.$$

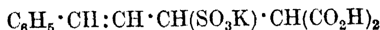
Sorbic acid (p. 172) yields $CH_3\cdot CH_2\cdot CH:CH\cdot CH_2\cdot CO_2H$; similarly butadiene, $CH_2:CH\cdot CH:CH_2$, reacts with bromine, yielding 1:4-dibromo-Δ^2-butene, $CH_2Br\cdot CH:CH\cdot CH_2Br$. Similar results have been obtained when the double bonds are between carbon and oxygen; thus benzil,



$$\overset{1}{O}:\overset{2}{C}(C_6H_5)\cdot\overset{3}{C}(C_6H_5):\overset{4}{O},$$

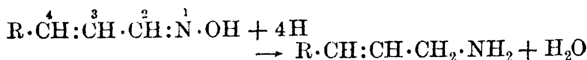
when reduced under special conditions yields $OH\cdot C(C_6H_5):C(C_6H_5)\cdot OH$ $\alpha\beta$-dihydroxy-stilbene.

That additions do not always take place in the 1:4-positions is shown by the following examples: Methyl cinnamylidene-malonate adds on bromine in the 3:4-positions and yields $C_6H_5\cdot CHBr\cdot CHBr\cdot CH:C(CO_2Me)_2$ (*Henrichsen* and *Triepel*, A. 1904, **336,** 223). The addition of potassium hydrogen sulphite to cinnamylidenemalonic acid occurs in the 1:2-position, and the product is:



$$C_6H_5\cdot CH:CH\cdot CH(SO_3K)\cdot CH(CO_2H)_2$$

(*Kohler*, Am. 1904, **31,** 243); similarly with hydrogen cyanide. Unsaturated aldoximes and ketoximes when reduced yield unsaturated amines, indicating that the addition of hydrogen—

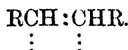


$$R\cdot\overset{4}{C}H:\overset{3}{C}H\cdot\overset{2}{C}H:\overset{1}{N}\cdot OH + 4H \rightarrow R\cdot CH:CH\cdot CH_2\cdot NH_2 + H_2O$$

occurs in the 1:2-position (*Harries*, A. 1903, **330,** 193); $\alpha\beta$ unsaturated ketones also add on sulphinic acids in the 1:2 (carbonyl) position (Am. 1904, **31,** 163). *s*-Diphenylbutadiene, CHPh:CH·CH:CHPh, also adds on bromine in the 1:2-position.

Thiele (A. 1889, **306,** 87) has attempted to account for the characteristic 1:4-addition of most of the compounds with conjugated double bonds by his theory of *partial valencies.*

It is supposed that when two atoms are united by a doublo bond the whole of the energy of the atoms is not used up, but that there is a slight residual affinity or *partial valency* which *Thiele* denotes by dotted lines, *e.g.*:



He considers the power of forming additive compounds is due to the presence of such partial valencies.

Now in a system with two double bonds in positions 1:2 and 3:4 there are four partial valencies, and according to *Thiele* two of these, viz. 2 and 3, are supposed to have neutralized one another and only 1 and 4 are active. This is usually represented by the formula—



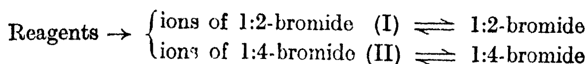
and hence the usual 1:4-addition with compounds containing conjugated double bonds. *Thiele's* theory does not account for the numerous exceptions mentioned above.

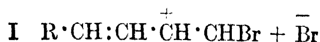
Probably it is simpler to regard the compound as containing 4 residual valencies in the 1, 2, 3, 4 positions, and to conclude that the question as to which of these will be used up in the formation of an additive compound depends largely on the nature of the addenda and the nature of the groups already attached to the atoms numbered 1, 2, 3, and 4.

The reaction between compounds with conjugated double bonds and Grignard's reagents consists in many cases of 1:4 addition. See *Kohler* (Am. 1904, **31**, 642; 1905, **33**, 21, 35, 153, 333; **34**, 568; 1906, **35**, 386; **36**, 177, 529; 1907, **37**, 369; **38**, 511; 1910, **43**, 412, 475).

Gillet (Bull. Soc. Bel. 1922, **31**, 366) concludes that in the case of the addition of bromine to a conjugated system, 1:2-addition always occurs as the first change, and that the 1:4-additive compounds sometimes isolated are due to anionotropic change (p. 760), resulting in the wandering of a bromine atom, probably as an ion, from position 2 to 4. *Farmer* and his co-workers support this view, and have shown that it holds good in the case of $\Delta^{1:3}$ cyclohexadiene and cyclopentadiene (J. C. S. 1929, 172), as unstable 1:2-dibromides are formed which can change into more stable 1:4 compounds. The slow

isomerization of certain 1:2-dibromides (J. C. S. 1928, 729) indicates that probably all 1:4-additive compounds cannot be formed by the change. *Ingold* (Rep. 1928, 132; 1929, 120) regards the addition as ionic and represents it by the scheme:


Reagents → {ions of 1:2-bromide (I) ⇌ 1:2-bromide; ions of 1:4-bromide (II) ⇌ 1:4-bromide}

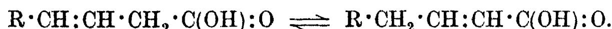

I $R\cdot CH:CH\cdot \overset{+}{C}H\cdot CHBr + \overset{-}{Br}$


II $R\cdot \overset{+}{C}H\cdot CH:CH\cdot CHBr + \overset{-}{Br}$

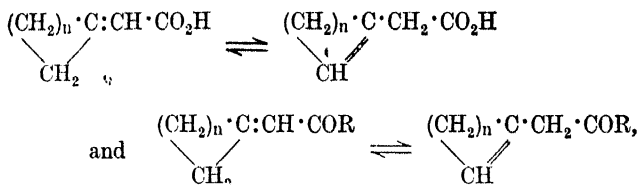
If conditions are not favourable to ionization the ions I unite rapidly to form the 1:2-bromide, otherwise equilibrium between I and II occurs and finally a mixture of 1:2- and 1:4-dibromides is obtained. Cf. also *Henrichsen*, Chem. Zeit. 1901, **316**, 43; *Chandrasena* and *Ingold*, J. C. S. 1922, 1310; *Farmer*, *Laroia*, *Switz*, and *Thorpe*, 1927, 2937; *Farmer*, *Lawrence*, and *Thorpe*, 1925, 729.

For differences met with in additions of hydrogen and bromine and an electronic representation of these, cf. Rep. 1929, 120.

Compounds containing two pairs of double linkings which are not conjugated frequently undergo molecular rearrangement, under suitable conditions yielding isomeric products with conjugate linkings. A simple example of this is met with in the conversion of $\beta\gamma$- unsaturated acids into $\alpha\beta$- unsaturated acids under the influence of alkalis (p. 168)—


$$R\cdot CH:CH\cdot CH_2\cdot C(OH):O \rightleftharpoons R\cdot CH_2\cdot CH:CH\cdot C(OH):O.$$

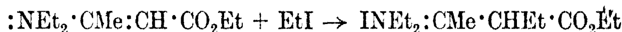
This equilibrium first established by *Fittig* has been examined in detail by *Linstead* and his co-workers, who show that the same equilibrium is attained from either side, but at quite different rates, and that the change is influenced by many factors, including the type of the solvent and the character of the radical R (J. C. S. 1927, 362; 2565, 2579; 1928, 2343; 1929, 2153, 2498. The composition of the equilibrium mixture was ascertained by addition of bromine or iodine, cf. J. C. S. 1927, 2565). The equilibrium has also been studied in the case of cyclic acids and ketones of the types



where n = 3, 4 or 5 and R = Me or Et, and also corresponding nitriles. (Rep. 1927, 117.) These phenomena are usually grouped with those of tautomeric change.

Another example is the conversion of aromatic compounds containing the $\cdot CH_2\cdot CH:CH_2$ into the isomerides containing the $\cdot CH:CH\cdot CH_3$ group, *e.g.* eugenol (p. 437), into isoeugenol; in this process the C:C of the side chain becomes conjugate with an olefine linking of the benzene nucleus.

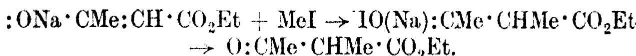
According to *Robinson* (J. C. S. 1916, **109,** 1038) an olefine linking can form a conjugate system with a tervalent nitrogen atom; thus in the addition of methyl iodide to ethyl diethylamino-crotonate, addition occurs at the ends of the conjugate system:



$$:NEt_2\cdot CMe:CH\cdot CO_2Et + EtI \rightarrow INEt_2:CMe\cdot CHEt\cdot CO_2Et$$

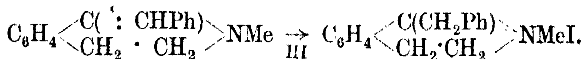
as on hydrolysis diethylamine hydriodide and ethyl α-acetylpropionate are formed, $INH_2Et_2 + O:CMe\cdot CHEt\cdot CO_2Et$.

It is highly probable that a bivalent oxygen atom can also form a conjugate system with an olefine linking, and the reaction of methyl iodide with the sodium derivative of ethyl acetoacetate may be regarded as an addition to the conjugate system:



$$:ONa\cdot CMe:CH\cdot CO_2Et + MeI \rightarrow IO(Na):CMe\cdot CHMe\cdot CO_2Et \rightarrow O:CMe\cdot CHMe\cdot CO_2Et.$$

An interesting example is the conversion of 1-benzylidene-2-methyl-tetrahydroisoquinoline into the methiodide of 1-benzyl-3:4-dihydro-isoquinoline:



D. Glutaconic Acids

Glutaconic acid, Δ^1-propene-1:3-dicarboxylic acid, $CO_2H\cdot CH:CH\cdot CH_2\cdot CO_2H$, exists in only one modification, and not in cis- and trans-isomerides.

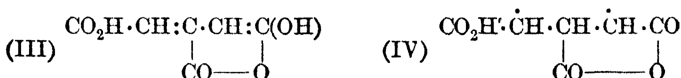
It has been proved that the 1 and 3 methyl-glutaconic acids are identical; also, the 1-methyl-3-ethyl acid is identical with the 3-methyl-1-ethyl acid, and the 1:2-dimethyl acid identical with the 2:3-dimethyl acid. This latter conclusion was arrived at by hydrolysing the following esters, $CO_2Et\cdot CMe(CN)\cdot CMe:CH\cdot CO_2Et$ and $CO_2Et\cdot CH(CN)\cdot CMe:CMe\cdot CO_2Et$, and obtaining the same dimethylglutaconic acid from both. These results point to a symmetrical formula for glutaconic acid and its alkyl derivatives, either $CO_2H\cdot \underset{\cdot}{CH}\cdot CH_2\cdot \underset{\cdot}{CH}\cdot CO_2H$ with two free valencies symmetrically placed, or



with a wandering hydrogen atom. *Thorpe's* researches point to the former conclusion. By the action of acetyl chloride on 1-methyl-glutaconic acid a hydroxy anhydride is formed which has the properties of a monobasic acid, and which can be hydrolysed by strong potassium hydroxide to a labile acid, m.-pt. 118°, which is converted by boiling with hydrochloric acid into the stable acid, m.-pt. 146°. This acid is also formed when the lactone is hydrolysed with water or dilute alkali. The labile acid is represented as a true olefinic acid with the *cis* structure, and all attempts to prepare the corresponding *trans* acid lead to the formation of the normal acid, to which is given the *s*-formula with free valencies. In the case of 1-benzyl-2-methylglutaconic acid the labile form isolated has the *trans* configuration, and so far the corresponding *cis* acid has not been prepared. The normal acid melts at 148° and the *trans* labile acid at 134°. The 3:3-dialkylated glutaconic acids, *e.g.* the dimethyl acid, $CO_2H\cdot CH:CH\cdot CMe_2\cdot CO_2H$, exist in the usual *cis* and *trans* forms, and exhibit no form analogous to the normal glutaconic acid. By the action of phosphorus pentachloride on monoalkylated glutaconic acids anhydrides of the type (I) are formed, but when these are distilled they yield the hydroxyanhydrides (II):

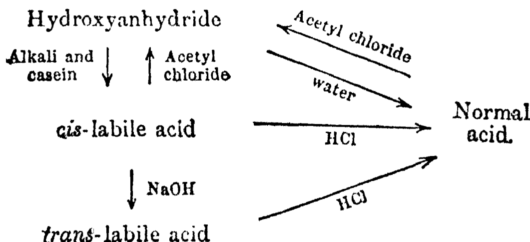


Aconitic acid (p. 271), $CO_2H\cdot CH:C(CO_2H)\cdot CH_2\cdot CO_2H$, may be regarded as a glutaconic acid substituted in position 2, and as such exists in the normal form $CO_2H\cdot \underset{\bullet}{C}H\cdot CH(CO_2H)\cdot \underset{\bullet}{C}H\cdot CO_2H$, which is the ordinary acid melting at 191°, and a labile *cis* form corresponding with the ethylenic formula and melting at 173°. The ordinary acid (m.-pt. 191°) with pure acetyl chloride yields the hydroxy anhydride (III), but with impure acetyl chloride or phosphorus trichloride the anhydride (IV) is obtained:



and it is the hydroxy anhydride (III) which yields the labile acid (m.-pt.) 173° when treated with strong alkali. The ordinary acid is formed by boiling the labile acid with dilute hydrochloric acid.

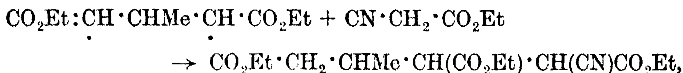
The *cis* configuration of the labile acid in the case of 1:3-dimethyl-glutaconic acid has been proved by its reduction to *cis*-dimethyl-glutaric acid under conditions which do not favour intramolecular change. In the case of 1-methyl-2-phenyl-glutaconic acid three isomers have been isolated corresponding with the normal, *cis* and *trans* configurations, and their mutual relationships are represented in the following scheme:



The esters of all the normal acids fail to condense with ethyl sodiocyanoacetate, whereas the esters of the labile acid can take part in such condensations. Similarly the labile

esters can be alkylated by means of sodium ethoxide and alkyl iodides, but the esters of the normal acids cannot. Such reactions can be used for deducing the structure of isomers.

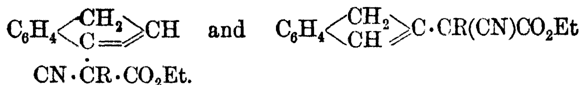
The labile esters and acids readily yield 1:2 addition products with bromine; the normal esters, on the other hand, do not appear to add on bromine in this manner, and no direct evidence of the 1:3 addition of bromine to the normal acids has so far been obtained. When, however, the condensation of ethyl 2-methylgutaconate with the sodium derivative of ethyl cyanoacetate is studied it is found that the *cis* labile ester gives an 80-per-cent yield of the normal condensation product (1:2 addition), cf. p. 841, and, under certain conditions, the normal ester gives a 6 per cent of a 1:3 addition product:



$$CO_2Et{:}\dot{C}H{\cdot}CHMe{\cdot}\dot{C}H{\cdot}CO_2Et + CN{\cdot}CH_2{\cdot}CO_2Et \rightarrow CO_2Et{\cdot}CH_2{\cdot}CHMe{\cdot}CH(CO_2Et){\cdot}CH(CN)CO_2Et,$$

which on hydrolysis yields 2-methylbutane-1:3:4-tricarboxylic acid, which can be synthesized by other methods. Although the yield of condensation product is small its formation is regarded as strong support for the symmetrical structure of the normal ester with free valencies in the 1:3 positions.

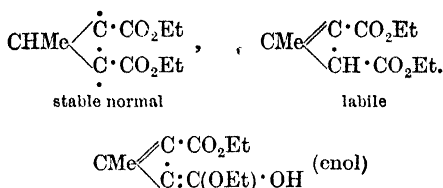
In the study of glutaconic acids it has been found that esters of the type $CO_2Et{\cdot}CR{:}CH{\cdot}CR'(CO_2Et)_2$ readily react with cold sodium ethoxide eliminating ethyl carbonate, $CO(OEt)_2$, and forming substituted glutaconic esters, $CO_2Et{\cdot}CR{:}CH{\cdot}CHR'{\cdot}CO_2Et$, which can exist in the ethenoid form and in the normal form. This elimination of CO_2Et of the ester with EtO of ethyl alcohol in the form of ethyl carbonate is characteristic of compounds which themselves cannot react as tautomers, but can as soon as the CO_2Et group is replaced by hydrogen, and a similar mobility holds good for the CO_2Et group in compound of the types:



$$C_6H_4{<}\genfrac{}{}{0pt}{}{CH_2}{C=}{>}CH \quad \text{and} \quad C_6H_4{<}\genfrac{}{}{0pt}{}{CH_2}{CH}{>}C{\cdot}CR(CN)CO_2Et$$
$$CN{\cdot}\dot{C}R{\cdot}CO_2Et.$$

J. F. Thorpe and others, J. C. S. 1913, 276, 1572; 1919, 143, 679; 1923, 62.

The cyclic ester diethyl 1-methyl-Δ^1-cyclopropene-2:3-dicarboxylate exists in three forms,



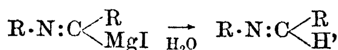
(J. C. S. 1923, 327, 3342.)

E. Compounds of Di- and Trivalent Carbon

1. **Carbon monoxide** may be written either as C:O or C⋮O. The first formula is the more probable as (*a*) a linkage C⋮O is difficult to represent spatially, and (*b*) when the monoxide forms additive compounds the two addenda become attached to carbon and not one to carbon and one to oxygen. Thus with chlorine we get carbonyl chloride, $O:C:Cl_2$, the constitution of which is determined by the fact that it reacts with alcohol, forming ethyl chloro-carbonate and finally ethyl carbonate, $O:C(OEt)_2$. With sodium hydroxide carbon monoxide gives rise to sodium formate: O:C + NaOH = O:CH(ONa), and with hydrogen chloride it yields the unstable formyl chloride, $O:C\begin{smallmatrix}H\\Cl\end{smallmatrix}$. Although vapour-density determinations indicate that in a mixture of the two gases very little combination has taken place, yet *Gatterman's* synthesis of aldehydes (B. 1897, **30**, 1622), by the action of a mixture of carbon monoxide and hydrogen chloride on aromatic compounds in the presence of aluminium chloride, proves that a small amount of an additive compound exists, and that its structural formula is the one represented above.

2. **Carbylamines.**—On p. 107 the conclusion has been drawn that in the carbylamines (alkyl isocyanides) the alkyl group must be attached to nitrogen and not to carbon, and therefore they are to be represented as R·N⋮C or R·N:C. In the latter formula the carbon atom is represented as being divalent, and the arguments used in support of this formula are similar to those used in the case of carbon monoxide, viz. (*a*) stereochemical considerations, and (*b*) the two addenda invariably unite with the carbon atom and not one

with carbon and one with nitrogen. The following examples can be given:—(*a*) with chlorine: $RN:CCl_2$; (*b*) with acyl chlorides: $R\cdot N:C\langle^{COPh}_{Cl}$; (*c*) with hydrogen sulphide $R\cdot N:CH\cdot SH = R\cdot NH\cdot CH:S$ (an alkylated thioformamide); (*d*) with oxygen: $R\cdot N:C:O$, alkyl isocyanates; (*e*) with sulphur: $R\cdot N:C:S$, mustard oils; (*f*) with *Grignard* reagents:



$$R\cdot N:C\langle^{R}_{MgI} \xrightarrow[H_2O]{} R\cdot N:C\langle^{R}_{H},$$

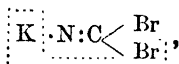
an imino-derivative which is hydrolysed to an aldehyde, $O:CH\cdot R$; (*g*) with ethyl hypochlorite. Cf. *Nef*, A. **270**, 267; **287**, 265.

Attempts have been made to represent carbylamines and other divalent carbon compounds by electronic formulæ, e.g. an alkylcarbylamine by the chemical formula, $R - N \rightleftharpoons C$, corresponding with the electronic formula, $R = \overset{+}{N} \vdots\vdots \overset{-}{C}^{2}$ (cf. Chap. XLVII, F.).

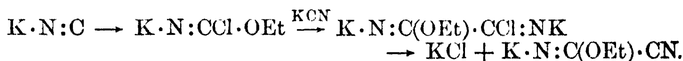
Both N and C have the complete octets, but of the 6 electrons shared by N and C four are derived from the nitrogen and only two from the carbon, so that carbon retains two unshared electrons and at the same time has a negative and nitrogen a positive charge. Such a formula is supported by a study of the parachors of such compounds and also by a study of their dipole moments (*Hammick*, *New*, *Sidgwick* and *Sutton*, J. C. S. 1930, 1876).

3. **Metallic Cyanides.**—Both nitriles and carbylamines are alkyl derivatives of hydrogen cyanide, and can be obtained by the action of alkyl iodides or potassium alkyl sulphates on different metallic cyanides, *e.g.* potassium cyanide and ethyl iodide yield ethyl cyanide, whereas the same iodide with silver cyanide yields mainly ethyl carbylamine. Although two series of alkyl derivatives exist, only one hydrogen cyanide is known. Certain of its reactions point to the nitrile structure $H\cdot C\vdots N$, and others to the carbylamine formula $H\cdot N:C$; it is a typical tautomeric substance. The view generally held with regard to the metallic cyanides is that they have a carbylamine structure. The arguments used are briefly as follows:—(1) The similarity between the additive reactions of metallic cyanides and those of carbylamines; (*a*) with bromine potassium cyanide yields potassium bromide and cyanogen

bromide; although an additive compound cannot be isolated, the reaction is in complete harmony with the view that an unstable compound,

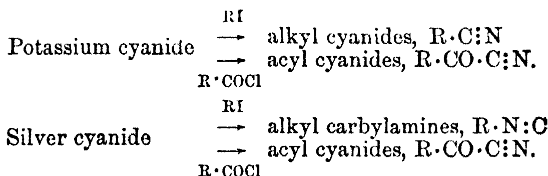


is formed which breaks up into KBr and N ⋮ C·Br; (*b*) potassium cyanide and benzoyl chloride yield benzoyl cyanide, N ⋮ C·CO·C_6H_5, but here again an additive compound, K·N:CCl·COC_6H_5, is probably first formed; (*c*) potassium cyanide combines with oxygen and sulphur in much the same manner as the carbylamines; (*d*) with ethyl hypochlorite a compound, HN:C(OEt)·CN, *ethyl cyano-imino-carbonate*, is formed. The reaction can be represented as follows:—



(2) Both alkyl carbylamines and alkali cyanides dissolve silver cyanide yielding double salts, whereas alkyl cyanides do not. (3) Tetramethylammonium cyanide, which probably has a constitution similar to that of the metallic cyanides, yields trimethylamine and methylcarbylamine when heated. This last argument by itself is of but little value, as a comparatively high temperature is required and molecular rearrangements could occur.

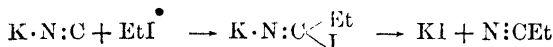
4. **Reactions of Metallic Cyanides. Formation of Nitriles and Carbylamines.** The following reactions occur:—



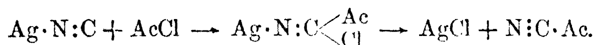
The reactions cannot be due to the tautomerism of silver cyanide, as no cases are known where a heavy atom like silver can wander. The view that carbylamines are first formed by simple exchange in all cases, and then in three of the four reactions the carbylamine becomes transformed into a nitrile, is untenable, as carbylamines cannot be transformed

into nitriles. The reverse process is also improbable, as carbylamines are formed from nitriles at high temperatures only.

The views of *Nef* (A. **287**, 274) as modified by *Wade* (J. C. S. 1902, 1596) are that in all four cases additive compounds are first formed. When the metallic radical in the cyanide is feebly positive, then feebly positive alkyl compounds combine with N, but negative acyl derivatives combine with C. With a strongly positive metallic atom in the cyanide, *e.g.* KCN, both alkyl and acyl derivatives combine with N. Thus with AgNC and EtI we have addition to N. Similarly with EtNC and EtI; but with AgNC and AcCl, and EtNC and AcCl, we have addition to C. With KNC and EtI and also with KCN and AcCl the addition is to C.







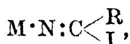
It may appear remarkable that in reaction 2 the alkyl iodide adds on to the nitrogen atom and leaves the carbon divalent. *Nef* assumed that the conversion of the silver salt into carbylamine was an example of direct displacement, but *Wade* proves that dry silver cyanide is able to absorb methyl iodide at its boiling-point, yielding a viscid mass which evolves methylcarbylamine when more strongly heated. The constitution of this additive compound is based on a study of the products from alkyl iodides and alkylcarbylamines; when hydrolysed these compounds yield *small amounts* of secondary amines, and hence, according to *Wade*, must be represented as: Me·N:C / Me⟋⟍I, and similar formulæ are given to the products from silver cyanide and alkyl iodides.

Hartley (J. C. S. 1916, **109**, 1296) represents the salts as bimolecular, as the first product of addition is $(AgCN)_2CH_3I$, followed at a higher temperature by $(AgCN, CH_3I)_2$. The formulæ of the metallic cyanides are written as K·N:C:NAg:C and AgN:C:NAg:C. With methyl iodide addition takes place at the $\overset{(1)}{N}$ atom (1), yielding

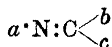


which decomposes into AgNC and $\genfrac{}{}{0pt}{}{Ag}{I}\!>\!N(CH_3):C$, and the latter gives AgI + CH_3·N:C.

Sidgwick (P. 1905, 120) concludes that in all cases addition takes place at the carbon atom:



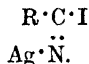
where M represents either K or Ag. Such a compound contains the grouping:



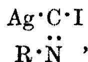
characteristic of the oximes of aldehydes and of unsymmetrical ketones (cf. pp. 143, 454), and can therefore exist in *syn*- and *anti*-configurations. Potassium cyanide is supposed to yield the *syn*-compound:



which readily loses potassium iodide, as both metal and halogen are on the same side of the molecule, and thus yields a nitrile. Silver cyanide, on the other hand, yields the *anti*-compound:



Silver iodide is not readily split off, as the metal and halogen are now on different sides of the molecule. It therefore undergoes the *Beckmann* transformation (p. 713), yielding:



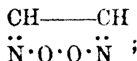
which loses silver iodide and forms C:N·R, an alkyl carbylamine.

Although the metallic cyanides are usually represented by a carbylamine structure, it does not follow that hydrogen cyanide is to be represented in a similar manner. Arguments based on a study of its physical and chemical properties have been brought forward; some point to the one, and others to the alternative formula, but probably, on the whole, the properties are more in harmony with the nitrile structure, **H·C⋮N.**

It is possible that it may be, like the tautomeric substance, ethyl acetoacetate, a mixture of the two compounds but mainly nitrile. (For summary see *Sidgwick*, " The Organic Chemistry of Nitrogen ", p. 209.)

The cyanides as salts are composed of ions whether in the solid state or in solution, and according to *Lowry*, *Sidgwick*, and others (J. C. S. 1930, 1884) both cyanides and isocyanides would yield the same anion $[^2C \equiv N^2]^-$ and hence there is no tautomerism between cyanide and isocyanide ions.

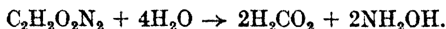
5. **Fulminic acid,** C:N·OH, is known chiefly in the form of its silver and mercury salts. The latter was first prepared in 1800 by *Howard*, by the action of alcohol and nitric acid on mercuric nitrate. It crystallizes in lustrous prisms, explodes with great violence when heated or struck, and is largely used in the manufacture of percussion caps, dynamite cartridges, &c. In 1824 *Gay-Lussac* and *Liebig* showed that the silver salt had the same percentage composition as silver cyanate, and thus afforded one of the first examples of isomerism. They also showed that double salts, *e.g.* $KAg(CNO)_2$, could be obtained. Various formulæ have been proposed. *Kekulé* suggested the formula NO_2·CH_2·CN, nitroacetonitrile; *Hollemann* suggested a glyoxime peroxide formula,



;

and *Steiner* in 1883 the formula OH·N:C:C:N·OH, di-isonitroso ethylene. It will be noticed that all these formulæ represented the molecule as containing two carbon atoms. The reasons for this were: (1) It is obtained from ethyl alcohol. (2) With bromine or iodine it yields ethane derivatives. (3) As it forms double salts the acid was thought to be dibasic. Various arguments were brought forward in favour of and against the first two formulæ, but the question has been definitely decided by the preparation of nitroacetonitrile (*Steinkopf* and *Bohrmann*, B. **41,** 1044) and of glyoxime peroxide (*Jovitschitsch*, A. **347,** 233), and showing that they differ from fulminic acid. The main argument in favour of *Steiner's* formula is that fulminates yield hydroxylamine when treated with concentrated hydrochloric acid, just as *V. Meyer* had previously shown that oximes do. *Steiner* was able to prove that the whole of the nitrogen can be removed in this

way in the form of hydroxylamine, and also that formic acid is the second product:



$$C_2H_2O_2N_2 + 4H_2O \rightarrow 2H_2CO_2 + 2NH_2OH.$$

Such a reaction proved that *Kekulé's* formula could not be correct.

In 1894 *Nef* (A. **280**, 303) suggested the simple formula C:N·OH, now generally accepted, which represents the acid as the oxime of carbon monoxide. The following arguments were adduced: (1) By the action of one equivalent of hydrogen chloride on one of the silver salt, no trace of silver chloride is formed, but an additive product, which was shown to be the chloride of formhydroxamic acid, or formyl-chloride oxime, Cl·CH:N·OH. This forms colourless crystals volatile at the ordinary temperature, and decomposes readily. With aniline it yields formanilide oxime, NHPh·CH:N·OH or NPh:CH·NH·OH. (2) It can be synthesised from a compound containing one carbon atom, namely nitromethane. The mercuric salt of nitromethane, when heated with water, yields water and mercury fulminate:



$$CH_2:NO{\cdot}OM \rightarrow H_2O + C:N{\cdot}OM.$$

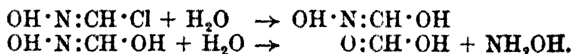
(3) With nitrous acid it yields methylnitrolic acid (p. 99).



$$C:N{\cdot}OH + H{\cdot}NO_2 \rightarrow NO_2{\cdot}CH:N{\cdot}OH.$$

(4) According to *Scholl* (B. **32,** 3492; **36,** 10, 322, 648), when benzene is treated with mercury fulminate and a mixture of anhydrous and hydrated aluminium chloride, benzaldoxime is formed (70 per cent). The water of the hydrated chloride liberates hydrogen chloride, which combines with the fulminate, yielding the additive compound, OM·N:CHCl, which then condenses with the benzene in the manner of the *Friedel-Crafts* reaction, yielding $C_6H_5{\cdot}CH:N{\cdot}OM$, from which the free oxime is liberated by means of mineral acid.

The hydrolysis of a fulminate to formic acid and hydroxylamine by means of hydrochloric acid is almost undoubtedly preceded by the formation of an additive compound:



$$OH{\cdot}N:CH{\cdot}Cl + H_2O \rightarrow OH{\cdot}N:CH{\cdot}OH$$
$$OH{\cdot}N:CH{\cdot}OH + H_2O \rightarrow O:CH{\cdot}OH + NH_2OH.$$

Free fulminic acid can be obtained by the action of an ex-

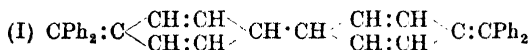
cess of sulphuric acid on a solution of potassium fulminate and extraction with ether. It volatilizes with the ether when this is distilled, and readily polymerizes to meta-fulminic acid. *Nef* has pointed out the remarkable analogy between hydrogen cyanide and fulminic acid. No direct estimations of the molecular weight of fulminic acid have been made, but an indirect determination by *L. Wöhler* (B. 1905, **38**, 1351) points to the simple formula HCNO. The method is based upon the determination of the value of *van't Hoff's* dissociation factor *i* for the sodium salt in 0·2 to 0·1 *N* solution. The value was found to be 1·85, the usual value for the salt of a monobasic acid. Also the increase in molecular conductivity in passing from *N*/32 to *N*/1024 solution was found to be 5 units, corresponding with *Ostwald's* value 4·8 for the salt of a monobasic acid.

The following has been suggested by *Wieland* as the probable course of the reaction in the preparation of a fulminate from ethyl alcohol: Oxidation to acetaldehyde, formation of isonitroso-acetaldehyde, oxidation to isonitroso-acetic acid, $HO \cdot N:CH \cdot CO_2H$, nitration to nitro-isonitroso-acetic acid, decomposition into carbon dioxide and methylnitrolic acid, conversion of methylnitrolic acid into nitrous and fulminic acids.

A polymer of fulminic acid, known as fulminuric acid, has been shown to be cyanonitroacetamide, $NO_2 \cdot CH(CN) \cdot CO \cdot NH_2$.

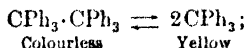
6. **Tervalent Carbon:** (*a*) *Triphenylmethyl.*—In attempting to prepare hexaphenylethane by the action of finely divided silver or zinc on triphenylchloromethane in benzene solution, *Gomberg* (J. A. C. S. 1900, **22**, 757) obtained a substance which contained oxygen, but in the absence of air the product was free from oxygen, and when the solution was carefully evaporated a compound with pronounced unsaturated properties was isolated. It combines vigorously with oxygen, yielding the **peroxide**, $CPh_3 \cdot O \cdot O \cdot CPh_3$, m.-pt. 185°–186°, which is transformed by sulphuric acid into triphenylcarbinol; it also combines with iodine, yielding triphenyliodomethane, and forms additive compounds with ethers, ketones, esters, nitriles, and with certain saturated hydrocarbons (J. A. C. S. 1915, **37**, 2569). It was suggested that these properties pointed to the formula, CPh_3, for the hydrocarbon, a formula which contains a tervalent carbon atom. The corresponding ion, $\overset{+}{C}Ph_3$, appears to be formed when triphenylchloromethane is dissolved in liquid

sulphur dioxide, as such solutions are good conductors of the electric current. Molecular weight determinations by the cryoscopic method point to the double formula, $(CPh_3)_2$, for the hydrocarbon. *Tschitschabin* (B. **37,** 4709) has suggested that the product is hexaphenylethane, and has supported this conclusion by a study of the properties of pentaphenylethane, which is somewhat unstable and readily attacked by oxygen, and is completely ruptured by hydrochloric acid at 150°. Quinonoid formulæ have also been suggested, the symmetrical formula I by *Heintschel* (B. **36,** 320, 579), and formula II by *Jacobson* (B. **37,** 196):

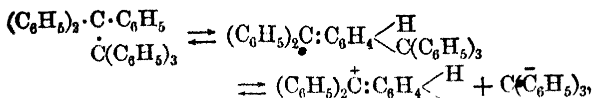




According to *Schmidlin* (B. **41,** 2471) two forms of triphenylmethyl exist, a colourless and a yellow. When freshly dissolved in benzene the solution is colourless but changes gradually to orange-yellow. The colour is destroyed by shaking the solution with air, but returns again on standing, and it is argued that the yellow form reacts with air more readily than the colourless compound. In solution there is an equilibrium between the colourless and coloured forms, and the equilibrium is displaced in favour of the colourless by lowering the temperature. The general view is that the equilibrium may be represented by the equation:



and this view is supported by *Wieland* (B. 1902, 3020), who shows that in naphthalene solution, which contains more of the yellow form than the benzene solution does, the molecular weight is much less than that required by the formula $(CPh_3)_2$, indicating that the yellow compound presumably has the composition CPh_3 (cf. *Piccard,* A. 1911, **381,** 347). *Gomberg* (B. 1913, 225; J. A. C. S. 1917, 1652; 1922, 1829; cf. *De,* J. C. S. 1919, 127) represents the equilibrium as not merely between the uni- and bi-molecular compounds, but also between benzene and quinonoid forms (cf. also B. **45,** 3171), and the dissociation of the latter into ions:



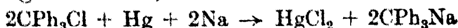
In the formation of additive compounds with oxygen, ethers, ketones, &c., it is probably the anion, $\bar{C}Ph_3$, which reacts, and the equilibrium between the ions is disturbed.

Schlenk and others (A. **372**, 1, **394**, 178) have prepared a **tri-diphenylmethyl**, $C(C_6H_4 \cdot C_6H_5)_3$, by the action of finely divided copper on tri-diphenylchloromethane, and have been able to show that in solution it is monomolecular. Solutions have a deep-violet colour, and it reacts readily with oxygen, giving a colourless peroxide. Corresponding diphenyl-diphenylmethyl, $\cdot CPh_2 \cdot C_6H_4 \cdot Ph$, phenyl-di-diphenylmethyl, $CPh(C_6H_4 \cdot Ph)_2$, and phenyl-diphenyl-α-naphthylmethyl, have been prepared; they exist in both coloured and colourless modifications. For diphenyl-α-naphthylmethyl see *Gomberg*, J. A. C. S. 1919, **41**, 1655; for thienyldiphenylmethane, ibid. 1913, **35**, 446, **41**, 16; and for general review of triphenylmethyl compounds, ibid. 1914, **36**, 1144.

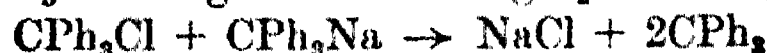
When the *p*-tribromo analogue of triphenylmethyl, viz. $(C_6H_4Br)_3C$, is examined it is found that one bromine atom behaves differently from the others, it is readily removed by means of metals, and hence presumably is differently situated in the molecule. This would agree with *Jacobson's* quinonoid formula, according to which the bromine atom (I) would be much more sensitive than the bromine atoms attached to the benzene atom (*Gomberg* and *Cone*, B. 1906, 771).



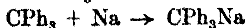
Compounds of the type of sodium triphenylmethane, CPh_3Na, have been prepared by *Schlenk* and *Marcus* (B. 1914, 1664). They cannot be obtained directly by the action of sodium on triphenylmethyl or triphenylchloromethane as the former is readily polymerised by sodium yielding *Ullmann* and *Borsum's* $CPh_3 \cdot C_6H_4 \cdot CHPh_2$ isomeric with hexaphenylethane (B. 1902, 2877). The sodium derivative is formed when sodium amalgam is used,



$$2CPh_3Cl + Hg + 2Na \rightarrow HgCl_2 + 2CPh_3Na$$

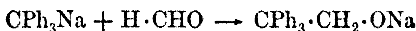


$$CPh_3Cl + CPh_3Na \rightarrow NaCl + 2CPh_3$$



$$CPh_3 + Na \rightarrow CPh_3Na$$

They are red solids sensitive to oxygen; with water, hydroxylic compounds or aldehydes and ketones which can react in an enolic form, they yield the original hydrocarbons, *e.g.* triphenylmethane; with CO_2 acids of the type of triphenylacetic acid, and with methyl iodide hydrocarbons, *e.g.* $CH_3 \cdot CPh_3$. With aldehydes or ketones incapable of reacting in the enolic forms, the sodium compounds react, yielding alcohols,



$$CPh_3Na + H \cdot CHO \longrightarrow CPh_3 \cdot CH_2 \cdot ONa$$

and in many respects resemble *Grignard* reagents, but are much more reactive (*Schlenk* and others, B. 1914, 1664; 1916, 608; 1922, 225), and with acid chlorides or esters of the type of ethyl benzoate they yield ketones, *e.g.* β-benzopinacoline $CPh_3 \cdot CO \cdot Ph$.

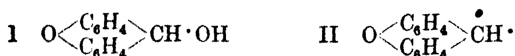
All the coloured metallic compounds of the type of triphenylmethyl when examined in dry ethereal solution are found to be good conductors of the electric current and are presumably ionized. Similarly with the coloured sodium compounds like sodium benzyl $NaCH_2 \cdot C_6H_5$ and the additive compound of sodium and stilbene; whereas the colourless compounds lithium phenyl, LiPh, &c., in ethereal solution are non-conductors.

We thus have CPh_3 the unionized radical, the kation $^+CPh_3$, both of which are yellow, and the anion $^-CPh_3$ red. The potassium salt is stable at ordinary temperatures. In anhydrous ammonia the metallic compounds are ionized (J. A. C. S. 1925, 2739). For reaction with nitrous oxide see *Schlenk* and *Bergmann*, A. 1928, **464,** 1, and for theoretical discussion of stabilities see *Burton* and *Ingold*, J. C. S. 1928, 907.

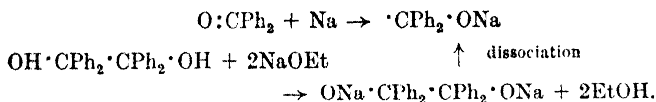
(*b*) *Other Tervalent Carbon Compounds.*—Just as colourless hexaphenylethane tends to break up into coloured triphenylmethyl, so pentaphenylethane when heated in anisole solution in absence of air breaks up into CPh_3 (yellow) and $CHPh_2$; the formation of the latter is proved by the formation of tetraphenylethane due to the union of two $CHPh_2$ radicals.

Conant and *Sloan* (J. A. C. S. 1923, 2446; 1925, 572, 1959, 3068) have obtained tervalent carbon compounds by the action of vanadous chloride on certain carbinols and oxonium salts; thus CPh_3 is readily obtained by the reducing action of the chloride on triphenylcarbinol in hydrochloric acid solution. When xanthenol (I) is used a pink precipitate of the radical

xanthyl (II) is formed, but this gradually polymerises to the colourless bi-xanthyl.



cf. also *Gomberg* and *Jickling*, J. A. C. S. 1913, 446. Other radicals which are capable of existing in the free state are $\cdot CPh_2 \cdot OPh$, $\cdot CPh_2 \cdot ONa$, $\cdot CPh(OPh)ONa$, $\cdot CHPh \cdot ONa$ (*Krans*, J. C. S. 1924, 2196), $\cdot C(C_6H_4 \cdot NO_2)_3$, (A. 1927, **458**, 248), and $\cdot CPh\langle^{CPh:CPh}_{CPh:\dot{C}Ph}$. Of these perhaps the most interesting are the **metal ketyls,** *e.g.* $\cdot CPh_2 \cdot ONa$, obtained by dissolving the metal in a diarylketone in an indifferent solvent or by the action of sodium ethoxide on a benzopinacone,


$$O{:}CPh_2 + Na \rightarrow \cdot CPh_2 \cdot ONa$$
$$OH \cdot CPh_2 \cdot CPh_2 \cdot OH + 2NaOEt \quad \uparrow \text{dissociation}$$
$$\rightarrow ONa \cdot CPh_2 \cdot CPh_2 \cdot ONa + 2EtOH.$$

Some are best prepared by double decomposition in dry ethereal solution between the ketyl $Ph \cdot C_6H_4 \cdot CPh \cdot OK$ and different ketones, *e.g.* dimethylpyrone.

All the metal ketyls are highly coloured. They are extremely reactive, thus they react readily with atmospheric oxygen yielding the original ketone and an alkali peroxide, iodine yields alkali iodide and ketone, water yields the ketone and the carbinol $CHR_2 \cdot OH$. With excess of sodium the ketyls yield disodium derivatives $Ph_2CNa \cdot ONa$, these are also coloured and react readily with oxygen or water, *e.g.*


$$Ph_2CNa \cdot ONa + 2H_2O \rightarrow Ph_2CH \cdot OH + 2NaOH,$$

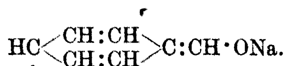
and with carbon dioxide yielding acids of the benzilic series


$$Ph_2CNa \cdot ONa + 2CO_2 \rightarrow Ph_2C(OH) \cdot CO_2Na + NaHCO_3$$

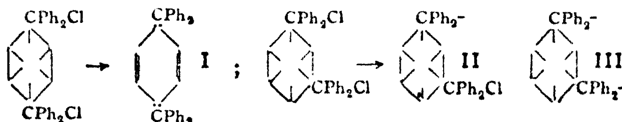
with methyl iodide the methyl ether of a tertiary alcohol is formed $Ph_2CMe \cdot OMe$, but this readily decomposes into the olefine $Ph_2C{:}CH_2$ and MeOH.

Benzaldehyde, ethyl benzoate and phenyl benzoate react with sodium yielding highly coloured metallic derivatives (*Blicke*, J. A. C. S. 1924, 2560; 1925, 229), probably $Ph \cdot CH \cdot ONa$

and Ph·CHNa·ONa probably in equilibrium with a quinonoid form

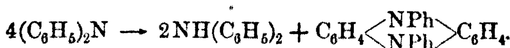


The two isomeric compounds, tetraphenyl-*m*- (and *p*) xylene dichlorides, $CPh_2Cl \cdot C_6H_4 \cdot CPh_2Cl$, behave quite differently when treated with metals. The *p*-compound readily yields the *p*-quinoid compound I (*Thiele* and *Balhorn*, B. 1904, **37**, 1463), whereas the *m*-compound loses either one or both chlorine atoms, yielding the triphenylmethyl derivatives II and III (*Schlenk* and *Brauns*, 1915, **48**, 661). These facts support the view that *m*-quinonoid compounds are incapable of existence.



For tervalent Silicon Compounds cf. *Kipping*, J. C. S. 1923, 2832; 1929, 2545.

(*c*) *Bivalent Nitrogen*.—For the existence of free radicals containing divalent nitrogen R_2N, cf. *Wieland* (A. 1911, **381**, 200; 1912, **392**, 127; 1913, **401**, 233), who shows that when a benzene solution of tetraphenylhydrazine is boiled for some time the chief products are diphenylamine and diphenyldihydrophenazine, which are regarded as formed from the radicals NPh_2:



Triphenylmethyl and tetraphenylhydrazine in benzene solution free from air yield **triphenylmethyldiphenylamine**, $CPh_3 \cdot NPh_2$. With nitric oxide in toluene solution it yields nitrosodiphenylamine $NPh_2 \cdot N{:}O$. Negative groups such as NO_2 militate against dissociation, whereas Me, OMe, and NMe_2 groups facilitate dissociation, as shown by molecular weight determination.

Probably in these hydrazines, as in the triphenylmethyl compounds, not only is there equilibrium between the radicals

and their polymers but also between benzenoid and quinoid forms, *e.g.* $PhN:C_6H_4<^{H}$, $PhN:C_6H_4<^{H}_{NPh_2}$.

Compounds of the type $NR_2\cdot NR\cdot$ also appear capable of existence (*Goldschmidt*, B. 1920, 44; 1922, 616; A. 1924, **437**, 194). They are termed **hydrazyls** and one of the most interesting is *aa-diphenyl-β-picrylhydrazyl*, $NPh_2\cdot N\cdot C_6H_2(NO_2)_3$, a stable crystalline solid with a colour similar to that of potassium permanganate, hydroquinone reduces it to the colourless hydrazine and the colour change is so sharp that the free radical can be estimated by titration with standard hydroquinone solution.

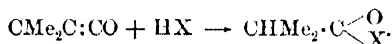
For examples of monovalent oxygen, *e.g.* $m\text{-}OMe\cdot C_6H_4\cdot O\cdot$, and the phenanthrene derivative $\begin{matrix} C_6H_4\cdot CCl \\ \vert \quad\quad \Vert \\ C_6H_4\cdot C\cdot O\cdot \end{matrix}$ see *Goldschmidt*, B. 1922, 3197; A. 1924, **348**, 202.

F. Ketens

Wilsmore (J. C. S. 1907, **91**, 1938; 1908, **93**, 946) has isolated the simplest possible ketone, $CH_2:CO$, which he terms **keten**, and which may be regarded as a new anhydride of acetic acid. It is obtained by the action of a hot platinum wire on acetic anhydride; numerous other substances are formed at the same time, but a 10-per-cent yield is obtained. It is a colourless gas at the ordinary temperature, has a characteristic odour, and reacts with hydrogen chloride, ammonia, and aniline, yielding acetyl chloride, acetamide, and acetanilide respectively. When kept for some time it polymerizes, yielding **cyclobutane-1:3-dione**, $CH_2<^{CO}_{CO}>CH_2$, b.-pt. 126°–127°, which combines with water to acetoacetic acid (p. 234), and with aniline to acetoacetanilide (J. C. S. 1910, 1978). The dione constitution is not accepted by *Schroeter* (B. 1916, **49**, 2697), who points out that true derivatives of the dione differ completely from these polymerization products.

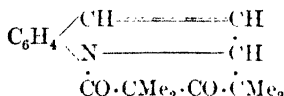
Homologues of keten, *e.g.* **dimethyl-keten** $(CH_3)_2C:CO$, and **diphenyl-keten**, $(C_6H_5)_2C:CO$ (*Staudinger*, B. 1905, **38**, 1735; 1906, **39**, 968; 1907, **40**, 1145, 1149; *Ott*, A. 1913, **401**, 159), have also been prepared. The method consists in the action of zinc on *a*-bromoisobutyryl bromide and diphenyl-chloro-

acetyl chloride respectively. The compounds are unstable and readily polymerize. Dimethyl-keten forms stable compounds with tertiary amines, and with water, alcohol, or amines gives isobutyric acid, its ester or amide:



The presence of a keten group, $\cdot CH_2\cdot CO\cdot$, is of great importance in the syntheses of numerous cyclic compounds (cf. *Collie*, J. C. S. 1907, **91**, 1806).

The homologues are frequently divided into (*a*) aldoketens, (*b*) ketoketens. The aldo group comprises keten, its monoalkyl substituted derivatives, and carbon suboxide. They are colourless, incapable of autoxidation, and are polymerized by pyridine. The keto group consists of the dialkylated derivatives. These are coloured, readily undergo autoxidation, and form additive compounds with tertiary amines, such as pyridine, quinoline, and acridine. These products from dialkyl ketens and tertiary amines are stable and have basic properties; they contain two molecules of keten combined with one of the base, and the compound with quinoline is represented as



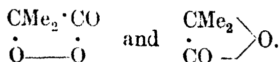
(A. 1910, **374**, 1). They also form additive compounds with substances containing the groupings C:N and C:O, for example, *Schiff's* bases and quinones. Diphenyl-keten and quinone yield the β-lactone, $O:C_6H_4\langle{}^{CPh_2}_{O\,—}\rangle CO$, which decomposes into CO_2 and $O:C_6H_4:CPh_2$, diphenyl-quinomethane, when heated (*Staudinger*, B. 1908, 905, 1355, 1493).

In the ketens the carbonyl group has not the same reactivity as in ordinary ketones, *e.g.* it does not form phenylhydrazones or semicarbazones. As seen above the olefine linking reacts readily with aldehydes and ketones, *i.e.* RHC:O and $R_2C:O$, the compounds formed are β-lactones, *e.g.*

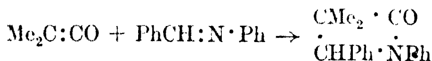


which are extremely unstable and decompose into tetra-alkylated olefines and CO_2.

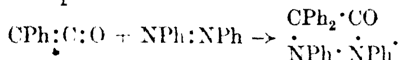
The autoxidation products are probably *e.g.*



With *Schiff's* bases the ketens combine to form stable β-lactams



and with azo compounds



The similarity in structure between an aldoketene R·CH:C:O and an alkyl isocyanate R·N:C:O corresponds with a certain similarity in chemical properties (*Stewart*).

Ethyl ethylketene-carboxylate, $CO_2Et·CEt:CO$, is colourless, and does not yield additive compounds, but readily polymerizes, yielding a cyclobutane derivative; but other carbethoxy ketenes are colourless, and yet form additive compounds with water, alcohol, or aniline (B. 1917, **50**, 1024).

G. Unsaturation and Physical Properties

Unsaturation, especially in the case of compounds with conjugate linkings, produces a marked effect on numerous physical properties. The phenomena which have been most closely studied are those on the refraction and dispersion of light. The effect of a conjugate linking such as that in CHMe:CH·CH:CHMe, is to produce a considerable increase or *exaltation* in the specific and molecular refraction and dispersion. In the case mentioned the molecular refraction is about one unit greater than the value calculated from the atomic refractions + two olefine linkings. The existence of such exaltation is frequently used as an argument in favour of the presence of conjugate linkings (either two olefine or an olefine and carbonyl) in the compound examined. In the case of hexatriene, CH_2:CH·CH:CH·CH:CH_2, the exaltation is 2·06 units. Exaltation is also observed when an acetylene linking is in conjugation with a carbonyl group. According to *Moureau* (Annales, 1906, [8],

7, 436), and *Müller* and *Bauer* (J. Chim. Phys. 1903, **1**, 190), the exaltation in certain series of compounds increases with the negative character of the substituents. Little or no exaltation is met with in the case of benzene, furane, diacetyl, and similar compounds, although the formulæ usually written for these compounds contain conjugate bonds. This may be due to special symmetrical ring structure or to mutual neutralization of residual affinities. Unsaturated groups such as amino, vinyl, and allyl, when present, in benzene compounds and directly attached to the nucleus, produce exaltation, probably owing to a readjustment of residual affinity. Exaltation is extremely well marked in compounds containing conjugate linkings, which, in their turn, are conjugate to the ethylene bonds in phenyl groups: *e.g.* diphenyl-butadiene, CHPh:CH·CH:CHPh, has an exaltation of 15 units (*Klages*, B. **40**, 1768); cinnamylideneacetic acid, CHPh:CH·CH:CH·C(OH):O, of 10·5 units, and diphenyl-hexatriene, CHPh:CH·CH:CH·CH:CHPh, of 24 units (*Smedley*, J. C. S. 1908, 376).

The enormous exaltations which phenyl groups produce on the molecular refractions of compounds like butadiene and hexatriene has been brought forward as an argument in favour of *Kekulé's* formula for benzene, as the three nuclear olefine linkings, which are themselves conjugate, are also conjugate with the olefine linkings in the diene or triene chain. On the other hand, benzene and its simple derivatives show little or no exaltation, and it is possible that the introduction of unsaturated side chains produces a change in the structure of the benzene ring itself.

Some of the most accurate work on unsaturated compounds has been carried out by *Auwers* and *Eisenlöhr* (J. pr. **82**, 65; **84**, 1, 37); *Auwers* and *Moosbrugger*, A. 1912, 387, 167; *Auwers* and *Ellinger*, ibid. 200, B. 1910, **43**, 806; 1911, **44**, 3514; 1912, **45**, 2764. They compare the specific refractions × 100, and not molecular refractions, and make use of the following values for atomic refractions n_D as determined by *Eisenlöhr* (Zeit. phys. **75**, 585); CH_2 = 4·618, C = 2·418, H = 1, O (in carbonyl) = 2·211, O (in ethers = 1·643, O (in hydroxyl) = 1·525, Cl = 5·967, Br = 8·865, I = 13·900, olefine linking = 1·733, and acetylene linking = 2·398. They find that a single conjugation in a hydrocarbon produces an exaltation of approximately 1·9 units, but that this value is reduced to an appreciable extent by the introduction of

substituents. The amount of this interference depends upon the number and position of the substituents. In cinnamene and its β-substituted derivatives the exaltation is about 1·0, and when three substituents are present the exaltation is only 0·45. They conclude that for a given type of compound the exaltation is fairly constant, and within such limits the existence of the exaltation may be made use of in discussions bearing on constitution.

Elements with residual valencies, *e.g.* N, S, Cl, when in conjugation with olefine linkings, also produce exaltation (*Eisenlöhr*, B. 1911, **44,** 3188; *Price* and *Twiss*, J. C. S. 1912, **101,** 1259).

When several pairs of conjugate linkings are present, it is found that the exaltation is much greater when these all form a single chain (cf. hexatriene) than when they are "crossed" as in $>C:C\begin{matrix} \diagup C:C \diagdown \\ \diagdown C:C \diagup \end{matrix}>$.

Semicyclic double bonds (p. 618) and rings formed of three atoms, *e.g.* trimethylene, also produce optical exaltation.

For effects of unsaturation on heats of combustion, see *Auwers* and *Roth* (A. **373,** 239, 267).

For effects of unsaturation on optical activity, see *Frankland* and others, J. C. S. 1906, 1854, 1861; 1911, 2325; *Hildich*, J. C. S. 1908, 1, 700, 1388, 1618; 1909, 331, 1570, 1578; 1910, 1091; 1911, 218, 224; Zeit. phys. 1911, **77,** 482; *Rupe*, A. **373,** 121.

Much work has been done on the relationship between colour and unsaturation. The quinonoid formulæ attributed to many dyes contain conjugate double linkings, and it is certain that the depth of colour tends to increase with the length of the conjugate chain of double linkings present in the compound. The auxo-chromic effects produced by amino and hydroxyl groups may also be due to the unsaturated nature of these groups.

II. Acetylenes

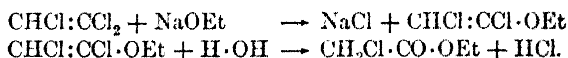
These hydrocarbons are highly unsaturated, and hence are extremely reactive, chemically, and within recent years numerous compounds of commercial importance have been synthesised from acetylene produced from calcium carbide (Chem. Trade J. 1919, **65,** 361). Among the most important

may be mentioned the hydration of acetylene to acetaldehyde in the presence of mercury salts (p. 136). A 99·9-per-cent aldehyde can be obtained by refrigeration and subsequent rectification. The aldehyde in its turn can be used for the production of (*a*) ethyl alcohol by mixing vapour with hydrogen and passing over finely divided nickel at 140°; (*b*) Acetic acid by oxidation with air in the presence of such catalysts as platinum, chromium and iron salts; (*c*) Ethyl acetate; (*d*) Paraldehyde; (*e*) Aldol and (*f*) acetic anhydride, *e.g.*:



$$2\,CH_3{\cdot}CH{:}O + Cl_2O \longrightarrow (CH_3{\cdot}CO)_2O + 2\,HCl.$$

The chlorination product, acetylene tetrachloride, is manufactured on a large scale by passing chlorine and acetylene into a porous material such as infusorial earth, or into $SbCl_5$. In this way explosions are avoided. The product known as **westron** is a heavy liquid with b.-pt. 147·2, and is used as solvent for cellulose acetate dopes. Trichlorethylene or **westrosol** is formed when the tetrachloride is passed over $BaCl_2$ or ThO_2 heated at 300°–390°. It is a liquid boiling at 88°, and is used for extracting oils from oil seeds and other materials. It is valuable, as it does not attack metallic vessels. Ethyl chloroacetate can be synthesised from trichlorethylene by treatment with alkali and alcohol; the first product is dichlorovinyl ether, which combines with water in the presence of a trace of HCl, forming ethyl chloroacetate:



$$CHCl{:}CCl_2 + NaOEt \longrightarrow NaCl + CHCl{:}CCl{\cdot}OEt$$
$$CHCl{:}CCl{\cdot}OEt + H{\cdot}OH \longrightarrow CH_2Cl{\cdot}CO{\cdot}OEt + HCl.$$

For production of thiophene cf. p. 552, and of isoprene, p. 611.

LI. ALIPHATIC DIAZO- AND TRIAZO-COMPOUNDS

A. **Diazo-** or **diazine compounds.**—By the action of nitrous acid on a solution of a salt of a primary aromatic amine of the type of aniline, the important group of diazo or diazonium salts are formed. It is generally stated that aliphatic amino-compounds and aromatic amines of the type of benzylamine differ from the true aromatic amines in this respect, and immediately yield the corresponding hydroxy-compounds. A few aliphatic amino-compounds do, however, yield diazo-derivatives with cold nitrous acid; one of the best known of these compounds is **ethyl diazo-acetate**, $\begin{matrix}N\\ \vdots\\ N\end{matrix}\!\!>CH\cdot CO_2Et$ (p. 220), a yellow oil, b.-pt. 141°. It differs from the aromatic diazonium salts in having both nitrogen atoms attached to carbon, and may be regarded as the anhydride of a diazo hydroxide, $OH\cdot N:N\cdot CH_2\cdot CO_2Et$. Not all aliphatic amines can yield diazenes, the essentials are that the carbon atom to which the amino group is united shall have a hydrogen atom attached to it, and also an unsaturated group, *e.g.* CO, CN. If these conditions are not fulfilled, no diazene can be isolated, and the product is an alcohol. Thus ethyl $\alpha\beta$-diaminopropionate with nitrous acid yields ethyl α-diazo-β-hydroxypropionate



$$NH_2\cdot CH_2\cdot CH(NH_2)\cdot CO\cdot OEt \rightarrow OH\cdot CH_2\cdot CN_2\cdot CO\cdot OEt.$$

It is probable that the H_2 of the $\cdot NH_2$ reacts with the O of $O:N\cdot OH$ yielding water and giving a diazo hydroxide. $\cdot N:N\cdot OH$ which then loses water giving the diazene.

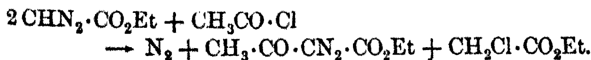
The ester is extremely reactive, and the N_2 group is readily replaced by I_2, HCl, H_2O, &c. With concentrated alkalis it yields **bis-diazo-acetic acid:**



$$CO_2H\cdot C\!\!<\!\!\begin{matrix}N & \text{——} & N\\ NH & \cdot & NH\end{matrix}\!\!>\!\!C\cdot CO_2H$$

(*Curtius*, *Durapsky*, and *E. Müller*, B. 1907).

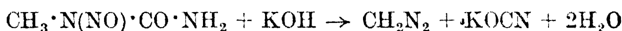
Ethyl diazoacetate reacts with acid chlorides, *e.g.* acetyl chloride, yielding ethyl chloroacetate and ethyl acetodiazoacetate:



$$2\,CHN_2\cdot CO_2Et + CH_3CO\cdot Cl$$
$$\rightarrow N_2 + CH_3\cdot CO\cdot CN_2\cdot CO_2Et + CH_2Cl\cdot CO_2Et.$$

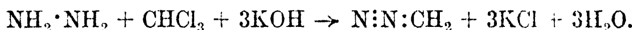
The diazo ester reacts with certain compounds containing olefine bonds yielding nitrogen and derivatives of cyclopropane (for examples cf. p. 630).

The simplest aliphatic diazo-compound is **diazo-methane,** $CH_2\!<\!\begin{array}{l}N\\ \cdot\cdot\\ N\end{array}$, which may be regarded as the anhydride of $CH_3\cdot N{:}N\cdot OH$. Diazo-methane is prepared by decomposing nitroso-methyl-urethane, $CH_3\cdot N(NO)\cdot CO_2Et$, with alkali, the compound, $CH_3\cdot N{:}N\cdot OK$, being formed as an intermediate product (*Hantzsch* and *Lehmann*, B. 1902, **35**, 897), or still more readily by decomposing nitrosomethylcarbamide with potassium hydroxide



$$CH_3\cdot N(NO)\cdot CO\cdot NH_2 + KOH \rightarrow CH_2N_2 + KOCN + 2H_2O$$

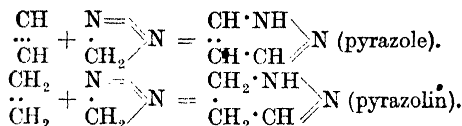
(*Werner*, J. C. S. 1919, 1093). A third method is by the action of chloroform and alkali on hydrazine



$$NH_2\cdot NH_2 + CHCl_3 + 3KOH \rightarrow N{:}N{:}CH_2 + 3KCl + 3H_2O.$$

It is a yellow, odourless gas at atmospheric temperature, and is excessively poisonous. It is characterized by its reactivity, and will readily convert acids into methyl esters, alcohols and phenols into methyl ethers, aniline and its homologues into secondary amines, and aldehydes into ketones, and is thus a valuable methylating agent. In all these reactions and also in the action of halogens, halogen hydracids, water, hydrocyanic acid and nitrogen peroxide, nitrogen is eliminated and two addenda unite with the carbon atom of the CH_2 (or substituted CH_2) group. The addenda are: acids $\cdot H$ and $\cdot O\cdot CO\cdot R$, alcohols $\cdot H$ and $\cdot OR$, amine $\cdot H$ and $RNH\cdot$, aldehydes $\cdot H$ and $\cdot RC{:}O$, halogens $\cdot Br$ and $Br\cdot$, water $\cdot H$ and $\cdot OH$, halogen hydracid $\cdot H$ and $\cdot Cl$, hydrocyanic acid $\cdot H$ and $\cdot C{\vdots}N$ or $\cdot H$ and $\cdot N{:}C$, nitrogen peroxide two $\cdot NO_2$ groups. With nitroso compounds of the type nitrosobenzene the divalent $:NPh{:}O$ replaces the N_2 and a nitrone, *e.g.* $Ph_2C{:}NPh{:}O$ is formed (Helv. 1919, 554) with sulphur dioxide diphenylmethyldiazene yields either benzophenone or tetraphenylethylenesulphone (B. 1916, 1941).

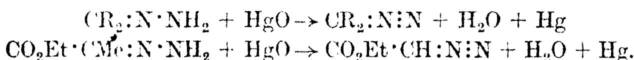
When reduced with hydrogen and colloidal platinum the diazenes yield hydrazones, *e.g.* $CPh_2{:}N\cdot NH_2$ (Helv. 1921, 21). It is also capable of uniting with unsaturated compounds, yielding heterocyclic derivatives, *e.g.*:



Cf. p. 562.

With thioketones, *e.g.* $Ph_2C:S$, and hydrocarbon diazenes an unstable compound $\begin{matrix}CPh_2\cdot S \\ \cdot \\ CPh_2\cdot N\end{matrix}\!\!>\!N$ is formed, which loses nitrogen, giving tetraphenylethylene sulphide, $\begin{matrix}CPh_2 \\ \cdot \\ CPh_2\end{matrix}\!\!>\!S$. (Helv. 1920, 833).

Numerous homologues of diazomethane and of ethyl diazoacetate have been prepared by *Staudinger* (B. 1916, **49**, 1884), some by the oxidation with HgO of the hydrazones derived from aldehydes and ketones



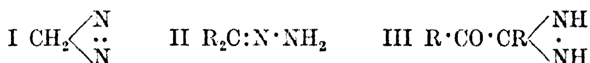
$$CR_2:N\cdot NH_2 + HgO \rightarrow CR_2:N:N + H_2O + Hg$$
$$CO_2Et\cdot CMe:N\cdot NH_2 + HgO \rightarrow CO_2Et\cdot CH:N:N + H_2O + Hg.$$

and diazoparaffins by the decomposition of nitroso-urethanes. $CMe_2:N_2$ is red and $CPh_2:N_2$, m.-pt. 29°, is bluish-red.

B. **Triazo-compounds.**—*Forster* (J. C. S. 1908, **93**, 72, 669, 1070, 1174, 1859, 1865) has obtained a number of fairly simple aliphatic triazo-derivatives containing the univalent grouping, $\begin{matrix}N \\ \vdots \\ N\end{matrix}\!\!>\!N\cdot$. *Ethyl triazo-acetate*, $N_3\cdot CH_2\cdot CO_2C_2H_5$, obtained by the action of sodium azide, NaN_3, on an alcoholic solution of ethyl chloro-acetate, is a colourless liquid, b.-pt. 44°–46° under 2 mm. pressure, and has a sweet odour suggestive of chloroform. From this ester *triazo-acetic acid*, m.-pt. 16°, and almost as strong an acid as bromo-acetic, and *triazo-acetamide*, m.-pt. 58°, have been obtained by the ordinary methods. *Triazo-acetone*, acetonyl-azoimide, $N_3\cdot CH_2\cdot CO\cdot CH_3$, obtained from chloro-acetone, is a colourless liquid, b.-pt. 54° under 2 mm. pressure. It has the properties of a ketone, *e.g.* yields a semicarbazone, m.-pt. 152°, and is instantly decomposed by alkalis. *Ethyl α-triazo-propionate* and the isomeric β-compound have been prepared, and also *α-triazo-propionic acid*, $CH_3\cdot CHN_3\cdot CO_2H$, the last of which has been resolved into optically active components. *Ethyl β-triazo-propionate* is so readily decomposed by alkalis that the corresponding acid and amide have not been prepared. *Allyl-azoimide*, $CH_2:CH\cdot CH_2\cdot$

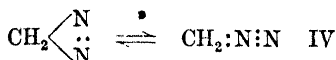
N_3, b.-pt. 76·5°; *triazo-ethyl alcohol*, $N_3 \cdot CH_2 \cdot CH_2 \cdot OH$, b.-pt. 60°/8 mm.; *triazo-acetaldehyde*, an oil, together with numerous esters derived from triazo-ethyl alcohol, have been prepared. Bis-triazo-compounds can be obtained, *e.g.* *bis-triazo-ethane*, $N_3 \cdot CH_2 \cdot CH_2 \cdot N_3$, and *ethyl bis-triazo-acetate*, $CH(N_3)_2 \cdot CO_2Et$, but are extremely explosive. Triazo-malonic acid and ethyl triazo-acetoacetate appear to be incapable of existence, but substituted derivatives, *e.g.* $CH_3 \cdot CO \cdot CN_3Me \cdot CO_2Et$, and even a bis-triazo-compound, $CH_3 \cdot CO \cdot C(N_3)_2 \cdot CO_2Et$, are known. *Triazo-ethylene*, $N_3 \cdot CH{:}CH_2$, can be obtained by eliminating hydrogen iodide from triazo-ethyl iodide. It is a pale-yellow liquid, b.-pt. 26°, and yields an oily dibromide. Numerous aromatic triazo-compounds have also been prepared, mainly from diazonium salts. (Cf. J. C. S. 1907, 855, 1350; 1909, 183; 1910, 126, 254, 1056, 1360, 2570.)

Differences of opinion on the structure of the diazene molecule still exist. The cyclic formula I was first suggested by *Curtius* and *Lang* (J. pr. 1892, [2], **44**, 554) mainly because the hydrazones of α-diketones differ in properties from the hydrazones of simple ketones; the former were represented by an open chain structure II, and the latter by ring formulæ III, and as these latter give diazenes on oxidation the cyclic



structure of the diazenes seemed probable. The examination of their absorption spectra by *Hantzsch* and *Lifschitz* (B. 1912, 3022) tended to confirm the ring structure. The non-cyclic structure of the hydrazones derived from α-diketones has been rendered highly probable by the work of *Forster* and *Zimmerli* (J. C. S. 1910, 2156) on camphor quinone, a typical α-diketone, $C_{18}H_{14}<{CO \atop CO}$, which yields two isomeric monohydrazones. These resemble one another so closely in chemical properties that they are undoubtedly stereoisomeric (geometrical isomerides) and therefore must be represented by the open chain structure, as the cyclic formula does not admit of stereoisomerism due to nitrogen part of the molecule. Hence the diazenes derived from the hydrazones have open chain formulæ (IV), as represented by *Angeli* and supported by *Thiele* (B. 1911, 2522).

The possibility of an extremely rapid tautomeric change



must not, however, be forgotten.

Practically all the chemical reactions of diazenes are in harmony with the open chain structure. This contains a quinquevalent nitrogen atom, and not the ordinary azo group as in diazobenzene; this group is generally reactive, yet in the numerous reactions of the aliphatic diazo-compound such a group does not take part (cf. *Forster* and *Cardwell*, J. C. S. 1913, **103**, 861; also *Staudinger*, B. 1916, **49**, 1884).

In a similar manner hydrazoic acid and its derivatives are represented by open-chain formulæ, *e.g.* HN:N⋮N. Such a structure accounts for the fact that by the action of *Grignard* reagents azides yield diazo-amino-compounds:



Parachors, on the other hand, are distinctly in favour of the cyclic structure (*Lindemann* and *Thiele*, B. 1928, 1529, cf. however, *Sidgwick*, J. C. S. 1929, 1108).

Carbon pernitride, CN_4, N⋮C·N:N⋮N, is formed by the action of cyanogen bromide on sodium azoimide. It forms colourless needles melting at 36°, explodes at 170°–180°, and its aqueous solution rapidly hydrolizes to hydrazoic acid and carbon dioxide (C. R. 1912, **154**, 1232).

Carbon subnitride, C_3N_2, obtained by heating tetraiodoglyoxalin (p. 564) at 420°. It is a brown-black amorphous substance, and in many respects resembles animal charcoal (B. 1913, **46**, 3129).

LII. SOME CYCLIC SYSTEMS

A. Synthesis and Degradation in Ring Systems

Most of the reactions discussed in the previous chapters have dealt with the conversion of derivatives of a given ring system into others containing the same ring, with the formation of cyclic from open-chain compounds, or with the conversion of ring into aliphatic derivatives.

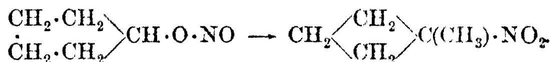
Reactions of considerable theoretical interest, which are occasionally met with, are the conversion of derivatives of one cyclic system into those of another containing one more or one less carbon atom in the ring.

1. DEGRADATION

As a rule when a ring compound without side chains undergoes isomerization the product formed is a ring containing a smaller number of carbon atoms, but with side chains.

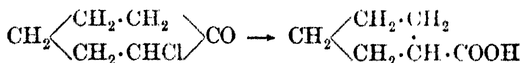
Thus cycloheptene when reduced gives methylcylcohexane and dimethylcylcopentane.

Also cyclopentyl iodide $\xrightarrow{AgNO_2}$ cyclopentyl nitrite $\xrightarrow{\text{Conc. KOH}}$ 1-nitro-1-methylcyclobutane:



And 2-iodo-cyclohexan-1-ol with silver nitrite yields 1-aldehydro-cyclopentane (C. R. 1914, **159**, 771).

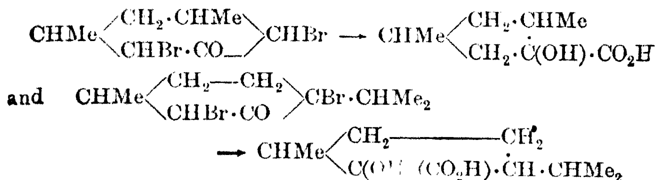
Many α-chlorinated cyclo-ketones react with alcoholic potash yielding acids derived from a lower ring system:



(J. russ. 1914, **46**, 1097).

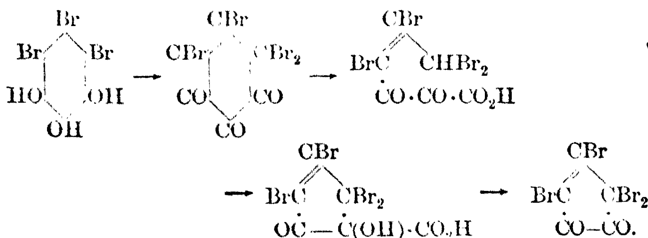
Wallach (A. 1918, **414**, 271) has studied the conversion of cyclohexanone into cyclopentanone derivatives. He shows that the dibromide formed from a cyclohexanone derivative in which the olefine linking is conjugate to the carbonyl group reacts with aqueous alkali yielding a phenol derived from cyclohexane, *e.g.* Δ^1-menthen-3-one yields 2-menthol.

With a dibromo-derivative in which the two bromine atoms are adjacent to the carbonyl group, but one on each side, the effect of alkali is to form a hydroxy-carboxylic acid derived from cyclopentane, and these can be readily oxidized to cyclopentanone derivatives, *e.g.*:



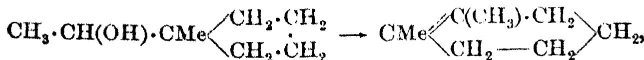
Meerwein (A. 1914, **405**, 129) shows that when water is eliminated from 1:1-dimethyl-Δ^1-cyclohexon-2-ol by means of oxalic acid the product is a mixture of 75 per cent of the dimethyl-Δ^1-cyclohexene and 25 per cent of isopropyl-Δ^1-cyclopentene. Cf. C. R. 1928, **186**, 375, 702; A. 1929, **477**, 99.

Xanthogallol, a product formed by the action of bromine water on the benzene derivative, tribromopyrogallol, $C_6Br_3(OH)_3$, is probably a cyclopentene derivative, and its formation can be represented by the following scheme (*Moore* and *Thomas*, J. A. C. S. 1917, **39**, 974):



2. SYNTHESIS

One of the smoothest of such changes is the conversion of 1-methyl-1-α-hydroxyethyl cyclopentane into 1:2-dimethyl-Δ^1-cyclohexene under the influence of zinc chloride:

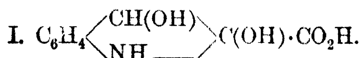


and similarly 1:2:2:3-tetramethyl-1-α-hydroxyethyl-cyclopen-

tane yields 1:2:3:3:4-pentamethyl-Δ^1-cyclohexene (*Meerwein*, A. 1918, **417**, 255).

The pinacone, $\left.\begin{matrix}CH_2\cdot CH_2\\ \cdot\\ CH_2\cdot CH_2\end{matrix}\right>C(OH)\cdot C(OH)\left<\begin{matrix}CH_2\cdot CH_2\\ \cdot\\ CH_2\cdot CH_2\end{matrix}\right.$, containing two cyclopentane rings, with dilute sulphuric acid yields a pinacoline, $\left.\begin{matrix}CH_2\cdot CH_2\\ \cdot\\ CH_2\cdot CH_2\end{matrix}\right>C\left<\begin{matrix}CH_2\cdot CH_2\\ CO\cdot CH_2\end{matrix}\right>CH_2$, in which the one cyclopentane ring has been transformed into a cyclohexane derivative. (*Meiser*, B. 1899, **32**, 2054.)

According to *Heller* (B. 1918, **51**, 424), an acid represented by formula I when oxidized with dichromate mixture yields the quinoline carboxylic acid II:





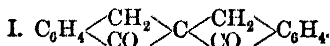
The number of carbon atoms in the ring is frequently increased when a ring compound containing side chains undergoes isomerization; thus 1-methyl-1-iodo-cyclopentane with silver nitrite yields a certain amount of the corresponding 1-nitro-1-methylcyclopentane, together with some nitrocyclohexane, and hydroxymethyl-cyclopentane with oxalic acid yields cyclohexene.

Isatin under the influence of diazomethane has its 5-membered N-ring changed into a 6-membered ring by the addition of CH_2 (para to NH), and the $\alpha\beta$ acetal of glycerol in the presence of a trace of acid gives the isomeric 2γ-acetal (change from 5 to 6 ring, each with two O).

The majority of these ring changes are probably due to an opening of the ring under the influence of the reagents, followed by ring closure.

B. Spirans

The combination of two rings with one carbon atom in common is termed a **spiran**, *e.g.* bis-1-hydrindone-2:2-spiran (I), and many such compounds have been examined by *Leuchs* and others (B. 1912, 189, 2114; 1913, 2420; 1915, 1432, 1531):



The two rings do not lie in the same plane. Compounds of the type $\frac{a}{b}\!>\!C\!<\!\frac{CH_2}{CH_2}\!>\!C\!<\!\frac{CH_2}{CH_2}\!>\!C\!<\!\frac{a}{b}$ should exist in optically active modifications. Cf. allene derivatives, $\frac{a}{b}\!>\!C\!:\!C\!:\!C\!<\!\frac{a}{b}$, p. 703.

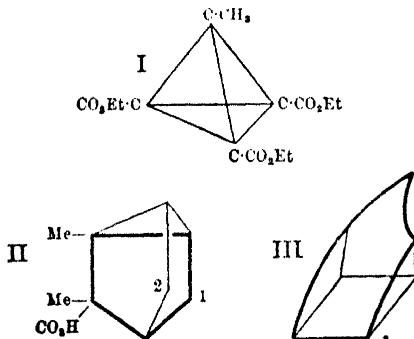
For stability of spiro compounds cf. *Thorpe* and others, J. C. S. 1915, **107**, 1080; 1919, **115**, 320; 1920, **117**, 1579.

C. Cage Systems

Just as a group of carbon atoms with attached hydrogen or other radicals can form a ring, so several rings can arrange themselves to form a **cage.**

A compound of this type prepared by *Beesley* and *J. F. Thorpe* (J. C. S. 1920, 617) is the one containing 3 cyclopropane rings, each with 2 carbon atoms in common, and so arranged as to form a tetrahedral cage (I). Teresantalic acid (II) is present in sandalwood oil, and has three cyclopentane rings with a basal C atom common to all, and forming a 3-carbon ring at the top. (Helv. 1926, 140.)

By a union of carbon atom 1 and 2 in (II) a new cage would be formed (III) with a basal 4 C ring, two side 3 C rings, and two 5 C atom rings, one in front and one behind. A typical cage is *Ladenburg's* prism formula for benzene (p. 361).



LIII. ORGANIC DERIVATIVES OF ARSENIC

In studying the various groups of carbon compounds, attention has already (pp. 90, 117, 119) been drawn to the fact that elements belonging to the same group in the periodic classification tend to give rise to similar types of organic derivatives.

Nitrogen, phosphorus, and arsenic belong to the same group, and hence the derivatives of arsenic should resemble those of nitrogen. Attention has already been drawn to such resemblances in the case of the arsines and arsonium compounds. The compound **pentamethylarsine,** $AsMe_5$, was described by *Cahours* in 1862 as an oily liquid, and it is only recently that analogous nitrogen compounds have been prepared by *Schlenk* and *Holtz* (Ber. 1916, **49,** 605; 1917, **50,** 274), for example, **benzyltetramethyl-ammonium,** $NMe_4 \cdot CH_2 \cdot C_6H_5$, cf. p. 407.

The chief groups of nitrogen compounds may be tabulated as follows:—

(*a*) Amines and alkylated ammonium salts.
(*b*) Nitroso- and nitro-derivatives.
(*c*) Azo and diazo-compounds.
(*d*) Nitriles and acid amides.
(*e*) Cyclic compounds with the nitrogen atom forming part of the ring.

So far arsenic derivatives corresponding with nitriles and acid amides have not been isolated.

The arsine oxides are analogous to the nitroso-compounds, *e.g.* phenylarsine oxide, $C_6H_5 \cdot As{:}O$, to nitrosobenzene, and *p*-hydroxyphenyl-arsine oxide, $OH \cdot C_6H_4 \cdot AsO$, to *p*-nitrosophenol.

The arseno-compounds are analogous to the azo-compounds,



and are at the present time compounds of commercial importance, as some of their derivatives find use as drugs (see Salvarsan). Aliphatic arseno-compounds of the type of arsenoethane, $C_2H_5As{:}AsC_2H_5$ (*Auger*, C. R. 1904, **138,** 1705), have

also been prepared, but appear to have the bimolecular formula $(AsEt)_4$.

A. ARYLARSINIC ACIDS

The **arylarsinic acids**, $R\cdot As\begin{smallmatrix}\nearrow O \\ - OH \\ \searrow OH\end{smallmatrix}$, comprise a group of great technical importance, as some of the substituted arsinic acids give rise to derivatives which possess considerable therapeutic value. Phenylarsinic acid, $C_6H_5\cdot As(OH)_2{:}O$, may be regarded as the hydrate of the arsenic analogue of nitrobenzene, and, when it is warmed, water is eliminated and the anhydride, $R\cdot As\begin{smallmatrix}\nearrow O \\ \searrow O\end{smallmatrix}$, is formed. The main difference between the nitrogen and arsenic compounds is that in the nitrogen series the anhydrides, $R\cdot NO_2$, are the stable compounds, the hydrates being unknown, whereas in the arsenic series the hydrates, $R\cdot AsO(OH)_2$, are the important compounds.

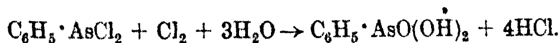
The arylarsinic acids are well defined crystalline substances, and in the majority of them the arsinic acid group is firmly attached to the benzene ring, so that the compounds may be used in a variety of different ways for synthetic purposes (*Ehrlich*). When reduced they can yield arsine oxides, $R\cdot As{:}O$, arseno compounds, $RAs{:}AsR$, or even primary arsines, $RAsH_2$, and thus resemble the nitro-compounds. They possess distinct acidic properties, yield soluble alkali salts and insoluble salts of heavy metals, but do not give precipitates with magnesia mixture in the cold; when heated, however, insoluble magnesium salts free from ammonia are formed.

A common synthesis of arsenic acids is by the action of arsenious acid or its salts on diazonium salts:



$$R\cdot N_2X + As(OH)_3 \rightarrow R\cdot AsO(OH)_2 + N_2 + HX.$$

Another method of formation is by the combined action of chlorine and water on chloroarsines (p. 120). (B. 1894, **27,** 265):



$$C_6H_5\cdot AsCl_2 + Cl_2 + 3H_2O \rightarrow C_6H_5\cdot AsO(OH)_2 + 4HCl.$$

A convenient method for preparing phenylarsinic acid itself is by the elimination of the amino-group from *p*-amino-phenylarsinic acid (*Bertheim*, B. 1908, **41,** 1855),

The esters of the arsinic acids can be prepared from the silver salts and alkyl iodides, and are disagreeably smelling liquids, which are readily hydrolysed when brought into contact with water.

The anhydride, $C_6H_5AsO_2$, obtained by dehydrating the corresponding acid at 140°, is a white amorphous powder; does not absorb moisture from the air, but dissolves in water yielding the acid.

Amino-derivatives of arylarsinic acids can be obtained by direct synthesis, namely, by heating a primary arylamine with arsenic acid:



$$C_6H_5{\cdot}NH_2 + O{:}As(OH)_3 = NH_2{\cdot}C_6H_4{\cdot}AsO(OH)_2 + H_2O.$$

In this reaction the $\cdot AsO_3H_2$ group always occupies the para position with respect to the amino-group, unless this position is already filled, when it takes up the ortho-position. A meta-amino-compound can be prepared by nitrating the unsubstituted arsinic acid and reducing the *m*-nitro acid by means of sodium amalgam and methyl alcohol; if other reducing agents are employed the arsinic acid group also is reduced.

p-**Aminophenylarsinic acid,** $NH_2{\cdot}C_6H_4{\cdot}AsO_3H_2$, is formed when aniline arsenate is heated. The process is usually termed arsenating—analogous to sulphonating—and the product is known as **arsanilic acid** (*Ehrlich* and *Bertheim,* B. 1907, **40,** 3292; *Benda,* 1908, **41,** 1674; 1909, **42,** 3621; *Kober* and *Davis,* J. A. C. S. 1919, **41,** 451). The reaction proceeds best at a temperature of 160°–185° and in the presence of an excess of aniline (3 mols:2 mols acid), but under no conditions is the yield a theoretical one. The arsenic acid appears to have an oxidizing action on the aniline, and red and black products are formed. A **diaminodiphenylarsinic acid,** $O{:}As(C_6H_4{\cdot}NH_2)_2{\cdot}OH$, is also formed as a by-product.

The amino group in these compounds is reactive and can be diazotized with the greatest readiness, and the diazo compounds so formed show the reactions characteristic of aromatic diazonium salts, including the formation of azo-dyes. The $\cdot AsO(OH)_2$ group is, on the whole, firmly united to the benzene ring, but can be readily replaced by iodine when the amino acid is warmed with potassium iodide and dilute sulphuric acid; in a similar manner arsanilic acid with bromine water yields *s*-tribromoaniline, a reaction analogous to that

between sulphanilic acid and bromine water. The replacement of the arsinic acid residue by iodine is frequently used for determining the relative positions of the substituents in aminoarylarsinic acids, *e.g.* *o*-arsinilic acid yields ortho-iodoaniline.* Free *p*-arsanilic acid is sparingly soluble in water or alcohol, but as an amphoteric substance dissolves readily in dilute mineral acids or alkalis. The mono-sodium salt was introduced into medicine in 1902 under the name of **Atoxyl,** and was the first aryl derivative of arsenic to find a therapeutic use. Recently an English firm has introduced a well-defined crystalline salt, $NH_2 \cdot C_6H_4 \cdot AsO(OH)(ONa), 5H_2O$, on the market under the name of **Soamin.** The stability of arsanilic acid towards sodium hydroxide solution at 100°–130° is interesting. With 1·5 mols. of alkali to one of the acid the solution is quite stable, and no hydrolysing action occurs; the maximum hydrolysis takes place when the ratio is 0·8:1. The replacement of the hydrogen atom of the second hydroxyl group thus has a stabilizing effect, and a similar result is obtained by acylating the amino group; the conclusion is drawn that the cause of instability is due to some interaction between the amino group and the second hydroxyl group (*Schmitz*, B. 1914, **47**, 363). For several years atoxyl was used in the form of intravenous injections in cases of anæmia, syphilis, elephantiasis, malaria, and other protozoal diseases, but has now been replaced by derivatives of tervalent arsenic of the salvarsan type which are far less toxic and dangerous. The poisonous effects of atoxyl are cumulative, and can lead ultimately to complete blindness and kidney complications.

Halogenated arsanilic acids can be obtained by the action of halogens in the absence of water, the halogen taking up the ortho position relative to the amino group. The mono-nitro derivative, 3-nitro-4-aminophenylarsinic acid, is best prepared by nitrating the oxalyl or urethane derivative, $H_2O_3As \cdot C_6H_4 \cdot NH \cdot CO \cdot CO_2H$ or $H_2O_3As \cdot C_6H_4 \cdot NH \cdot CO \cdot OEt$, and when reduced with alkaline hydrosulphite yields the *o*-diamine, 3:4-diaminophenylarsinic acid, which gives most of the reactions characteristic of *o*-diamines (p. 408).

As an amine atoxyl gives rise to a series of acyl derivatives, two of which are *monoacetylatoxyl* (arsacetin), $NHAc \cdot C_6H_4 \cdot$

*** Amino acids in which the amino-group is in the meta-position relative to the arsinic acid group are not decomposed by halogens or hydriodic acid.**

$AsO(OH)(ONa)$, $5H_2O$, and *sodium-4-benzenesulphonyl-1-amino-phenylarsinate* (pectine), $SO_2Ph\cdot NH\cdot C_6H_4\cdot AsO(OH)(ONa)$. Both of these were used at one time in medicine—as they are less toxic and more stable; for example, their solutions can be sterilized by boiling without undergoing decomposition—but have now been discarded.

With aldehydes arsanilic acid yields benzylidene and analogous derivatives, *e.g.* $OH\cdot C_6H_4\cdot CH:N\cdot C_6H_4\cdot AsO(OH)_2$, which are usually coloured and amphoteric in character.

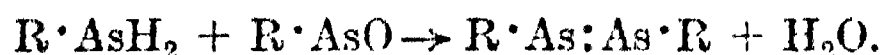
Numerous hydroxy derivatives of arylarsinic acids are known. ***p*-Hydroxyphenylarsinic acid,** $OH\cdot C_6H_4\cdot AsO(OH)_2$, obtained by heating phenol with arsenic acid (H_3AsO_4) at 150° (*Conant*, J. A. C. S. 1919, 431), or by diazotizing *p*-arsanilic acid and warming the solution, forms a crystalline mass readily soluble in water or alcohol.

Compounds obtained by condensing *p*-amino-phenylarsinic acid with amides, ureides or anilides of halogenated fatty acids are also valuable agents in treating trypanosomal and spirochætal infections (U. S. P.).

Tryparsamide, N-phenylglycineamide-4-arsinic acid, $NH_2\cdot CO\cdot CH_2\cdot NH\cdot C_6H_4\cdot AsO(OH)_2$, is the most effective organic arsenical for treatment of human sleeping sickness (J. A. C. S. 1919, 1589), and related compounds, *e.g.* N-phenylalanine amide-4-arsinic acid, $NH_2\cdot CO\cdot CHMe\cdot NH\cdot C_6H_4\cdot AsO(OH)_2$, have been examined by *Gibson* and others (J. C. S. 1929, 479). This latter acid was resolved into active components by means of quinine and the active acids tend to racemise during hydrolysis. Derivatives of diphenylaminearsinic acids, *e.g.* $NHPh\cdot C_6H_3(NO_2)\cdot AsO(OH)_2$ have been prepared by *Barber* (J. C. S. 1929, 471), and their trypanocidal activity examined.

B. DERIVATIVES OF ARSENOBENZENE

As already pointed out, the arseno-derivatives are the arsenic analogues of the azo-compounds, and they can be synthesised by a process analogous to the one described for the azo-compounds (No. 5, p. 425), namely, by condensing a primary arsine with an arsine oxide:



$$R\cdot AsH_2 + R\cdot AsO \rightarrow R\cdot As:As\cdot R + H_2O.$$

The usual method of preparing arseno-compounds of com-

mercial importance is by the reduction of arylarsinic acids, a reaction similar to the formation of azobenzene by the reduction of nitrobenzene.

In the case of nitro compounds the actual product obtained depends upon the reducing agent used and the conditions of reduction (pp. 422, 665, 683). A similar statement holds good for the arylarsinic acids. Metals and concentrated acids give rise to primary arsines; mild reducing agents, such as sulphurous acid with a little hydriodic acid, phenylhydrazine or phosphorus trichloride, give rise to phenylarsine oxides; whereas sodium hydrosulphite reduces the arsinic acids to arseno compounds.

The study of the action of reducing agents on compounds containing both nitro and arsinic acid groups has led to some interesting generalizations.

1. Sulphurous acid with hydriodic acid as catalyst, phenyl hydrazine, thionyl chloride or phosphorus trichloride give amino-arsine oxides, *e.g.* $NH_2 \cdot C_6H_4 \cdot As{:}O$.

2. A metal and strong acid, or electrolytic reduction, especially in the presence of methyl or ethyl alcohol, tends to give rise to amino primary arsines, $NH_2 \cdot C_6H_4 \cdot AsH_2$.

3. Ferrous hydroxide, or the theoretical amount of sodium amalgam, reduces the nitro group but leaves the arsinic acid group intact.

4. Phosphorous and hypophosphorous acids reduce the arsenical group but leave the nitro group intact, and give as products nitro-arylarseno compounds, $NO_2 \cdot C_6H_4 \cdot As{:}As \cdot C_6H_4 \cdot NO_2$, and the same result can be effected by stannous chloride activated by hydriodic acid.

5. Sodium hydrosulphite reduces the nitro- to an amino-group, and the arsenic acid radicle to the arseno-group, giving rise to the compound $NH_2 \cdot C_6H_4 \cdot As{:}As \cdot C_6H_4 \cdot NH_2$.

The arseno-group, $\cdot As{:}As \cdot$, unlike the azo-group, $\cdot N{:}N \cdot$, has but feeble chromorphoric effect, and the arseno derivatives are, as a rule, pale yellow in colour.

Arsenobenzene, $C_6H_5 \cdot As{:}As \cdot C_6H_5$, crystallizes in yellow needles, melts at 196°, and when strongly heated yields triphenylarsine and arsenic:



$$3\ PhAs{:}AsPh \rightarrow 2\ AsPh_3 + As_4.$$

It is decomposed by chlorine yielding $C_6H_5AsCl_2$, by sulphur yielding C_6H_5AsS, and by oxidizing agents yielding phenyl-

arsinic acid, but with iodine it forms an extremely unstable additive compound, $C_6H_5AsI \cdot AsIC_6H_5$, in the form of yellow crystals.

Numerous substituted derivatives of arsenobenzene are known, those containing hydroxy and amino, or substituted amino, groups being of greatest technical importance. Characteristic of these compounds is the readiness with which a mixture of two symmetrical arseno compounds is transformed into an unsymmetrical derivative (*Karrer*, B. 1916, **49**, 1648), *e.g.*:



$$RAs{:}AsR + R'As{:}AsR' \rightarrow 2\,RAs{:}AsR',$$

by heating to about 80° in the presence of water.

Derivatives of arsenobenzene have completely replaced the earlier quinquevalent arsenic compounds used in the treatment of protozoal diseases. They are not only more effective as destroyers of trypanosomes, but are much less toxic, and the possibility of injurious effects on the human body is reduced to a minimum.

The earliest derivative of therapeutic value was **Salvarsan,** 3:3′-*diamino*-4:4′-*dihydroxyarsenobenzene hydrochloride*, known also as **Kharsivan, Arsenobillon,** or " 606 ".*

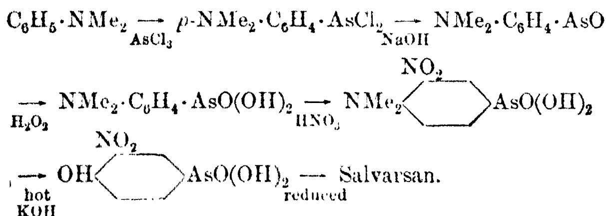
The starting-point for the preparation of salvarsan is *p*-arsanilic acid. This is diazotized in sulphuric acid solution, and the solution of the diazonium salt heated at 70°; the resulting *p*-hydroxyphenylarsinic acid nitrated with a mixture of nitric and sulphuric acids yields 3-*nitro*-4-*hydroxyphenylarsinic acid*, $OH \cdot C_6H_3(NO_2) \cdot AsO(OH)_2$ (B. 1911, **44**, 3445), whose constitution follows from the fact that it can be obtained by the diazo-reaction from *o*-nitro-*p*-aminophenol. When the nitro-hydroxy acid is reduced with sodium hydrosulphite at 55°–60° in the presence of magnesium chloride solution, care being taken that the mixture is well stirred, a microcrystalline, yellow precipitate of the diaminodihydroxyarsenobenzene is formed.

Salvarsan is made by dissolving the precipitate in methyl alcohol and adding the requisite amount of methyl alcoholic solution of hydrogen chloride. The commercial product con-

* It is stated that this compound was termed " 606 " by Ehrlich, as it was the 606th arsenic compound prepared by him in his attempts to obtain effective remedies for protozoal diseases.

taining one molecule of methyl alcohol forms a bulky yellow crystalline powder soluble in most solvents with the exception of acetone, ether or glacial acetic acid. A pure dihydrochloride free from methyl alcohol is colourless (*Kober*, J. A. C. S. 1919, **41**, 442). Like most derivatives of arsenobenzene, salvarsan is readily oxidized in contact with the air, yielding *3-amino-4-hydroxyphenylarsine oxide*, which is twenty times as toxic as salvarsan. Iodine or hydrogen peroxide oxidizes salvarsan to the corresponding arsinic acid. Derivatives of salvarsan in which the hydrogen atoms of the hydroxyl groups have been replaced by metallic radicles such as sodium or copper are of therapeutic use.

The following is an alternative method for preparing salvarsan:

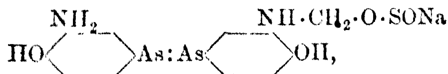


(Eng. Pat. 1914, 22,521).

Numerous alkylated chloro and nitro derivatives of salvarsan have been prepared, also arsenobenzenes containing as many as six amino groups in the molecule.

One of the chief objections to the use of salvarsan is that its aqueous solutions are distinctly acidic and have to be exactly neutralized with alkali just before intravenous injection.

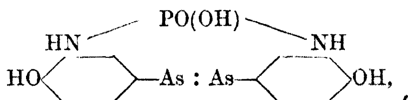
The substance **Neosalvarsan,** known also as **Neokharsivan** or **Novarsenobillon,** is free from this defect; it is the sodium salt of an N-methylsulphinic acid derived from salvarsan base, and is represented by the structural formula:



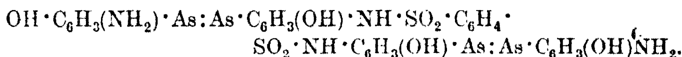
sodium 3:3′-diamino-4:4′-dihydroxyarsenobenzene-N-methylenesulphinate, and its aqueous solutions are neutral. Neosalvarsan

can be prepared by the action of sodium formaldehyde sulphoxylate on salvarsan, precipitating the free acid, dissolving the acid in dilute caustic soda solution, and precipitating the sodium salt by pouring into alcohol. The condensation appears to be facilitated by working in the presence of ethyl alcohol, ethylene glycol, or glycerol. It can also be prepared by the action of a warm aqueous solution of sodium formaldehyde sulphoxylate (2 pts.) on sodium 3-nitro-4-hydroxybenzenearsinate, or by the action of the same reagent on 3:3′-dinitro-4:4′-dihydroxyarsenobenzene.

Two compounds of the neosalvarsan type which have also been used are: (*a*) **Galyl,** the sodium salt of *4:4′-dihydroxy-arsenobenzene-3:3′-phosphamic acid*:



and (*b*) **Ludyl,** the sodium salt of *benzene-m-3:3′-disulphamino-bis-3-amino-4:4′-dihydroxyarsenobenzene*:


$$OH\cdot C_6H_3(NH_2)\cdot As:As\cdot C_6H_3(OH)\cdot NH\cdot SO_2\cdot C_6H_4\cdot SO_2\cdot NH\cdot C_6H_3(OH)\cdot As:As\cdot C_6H_3(OH)NH_2.$$

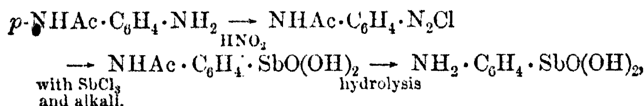
The former compound is made by condensing 3-amino-4-hydroxy-phenylarsinic acid with phosphorus oxychloride in the presence of aqueous sodium hydroxide solution, and reducing the condensation product with sodium hydrosulphite; and the latter of the condensation of salvarsan with benzene-*m*-disulphonic chloride by the ordinary *Schotten-Baumann* method. Both compounds are only slightly toxic, have energetic spirillicadal action and produce no serious after-effects.

Arsenobenzene and its derivatives form additive compounds with numerous salts of heavy metals, such as copper, silver, gold, mercury, and the platinum metals (*Ehrlich* and *Karrer*, B. 1915, **48,** 1634; *Danysz*, C. R. 1913, **157,** 644; 1914, **158,** 199, 452). These compounds are of the type, R·As:AsR, MeX, and R·As:AsR, 2MeX, and their formation is presumably due to the residual affinity of one or both arsenic atoms, as arsenobenzene itself, which contains neither hydroxyl nor amino groups, can form such derivatives (*Ehrlich*, B. 1915, **48,** 1634).

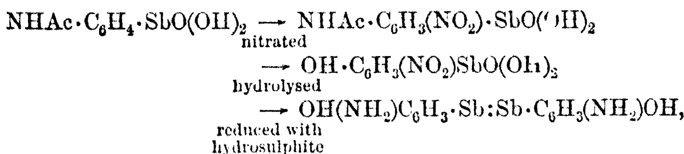
One of these additive or co-ordination compounds has been used medicinally, namely **luargol,** or 3:3′-*diamino-4:4′-dihydroxy-arsenobenzene-silver-bromide-antimonyl-sulphate* $[C_{12}H_{12}O_2N_2As_2]_2$, AgBr, $SbO(H_2SO_4)_2$, an additive compound of salvarsan base with silver bromide and antimonyl sulphate. It is neutralized with caustic soda previous to injection, and is stated to be ten times as active as salvarsan in cases of sleeping sickness.

Numerous derivatives of **stibinoarsenobenzene,** $C_6H_5Sb:AsC_6H_5$, have been prepared, *e.g.* the 4:4′-dihydroxy derivative, $OH \cdot C_6H_4Sb:AsC_6H_4 \cdot OH$, is obtained by reducing a mixture of sodium *p*-hydroxyphenylarsinate and *p*-hydroxyphenylstibinate, $OH \cdot C_6H_4 \cdot SbO(ONa)_2$, with sodium hydrosulphite, and forms a brownish-black powder insoluble in water. Of this type of compound 3-*amino-4-hydroxyarseno-4′-acetylamino-stibinobenzene hydrochloride*, HCl, $NH_2 \cdot C_6H_3(OH)As:SbC_6H_4 \cdot NHAc$, gives the best therapeutic results.

The antimony analogues of atoxyl and salvarsan are also known, and can be prepared by the following series of reactions:



the antimony analogue of atoxl.

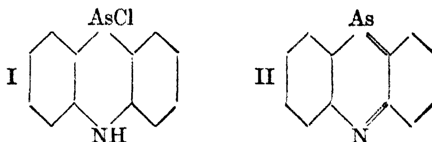


the antimony analogue of salvarsan.

Sulphoform, *triphenylstibine sulphide*, $S:SbPh_3$, colourless needles melting at 119°–120°, obtained by passing sulphuretted hydrogen cautiously into a solution of triphenylstibine chloride in alcoholic ammonia, is used in pharmacy for curing eczema and similar skin diseases.

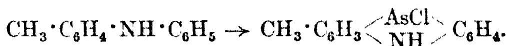
C. CYCLIC ARSENIC COMPOUNDS

Derivatives of 10-*chloro*-5:10-*dihydrophenarsazine* (I)



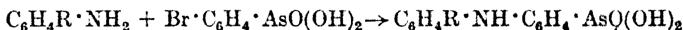
have been prepared by *Gibson* and others (J. C. S. 1926–29; cf. also *Wieland* and *Rheinheimer*, A. 1921, **423**, 1) using three different methods.

The compounds are interesting as containing an arsenic atom as part of a ring, and the parent substance, phenarsazine, is represented by formula II: (*a*) The condensation of arsenious chloride with substituted diphenylamines in suitable solvents, *e.g.*:



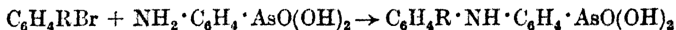
$$CH_3 \cdot C_6H_4 \cdot NH \cdot C_6H_5 \rightarrow CH_3 \cdot C_6H_3 < \begin{matrix} AsCl \\ NH \end{matrix} > C_6H_4.$$

(*b*) the elimination of hydrogen bromide from *o*-bromo-*o'*-amino diphenylarsinic acid $\begin{matrix} C_6H_4Br \\ NH_2 \cdot C_6H_4 \end{matrix} > AsO(OH)$, the bromine forming hydrogen bromide with one of hydrogens of the amino-group, and a phenarsazinic acid $C_6H_4 < \begin{matrix} AsO(OH) \\ NH \end{matrix} > C_6H_4$ is formed; (*c*) the condensation of *o*-bromo-phenylarsinic acid with substituted amines



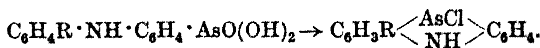
$$C_6H_4R \cdot NH_2 + Br \cdot C_6H_4 \cdot AsO(OH)_2 \rightarrow C_6H_4R \cdot NH \cdot C_6H_4 \cdot AsO(OH)_2$$

or the condensation of *o*-aminophenylarsinic acid with substituted bromobenzenes



$$C_6H_4RBr + NH_2 \cdot C_6H_4 \cdot AsO(OH)_2 \rightarrow C_6H_4R \cdot NH \cdot C_6H_4 \cdot AsO(OH)_2$$

and then ring closure of the product, obtained by either of these condensations, by means of hydrochloric acid, sulphur dioxide and iodine



$$C_6H_4R \cdot NH \cdot C_6H_4 \cdot AsO(OH)_2 \rightarrow C_6H_3R < \begin{matrix} AsCl \\ NH \end{matrix} > C_6H_4.$$

These cyclic dihydro compounds yield N acyl, but not N

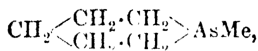
alkyl derivatives, and are characterized by the readiness with which they form molecular compounds with acetic acid, acetone, chlorobenzene, carbon tetrachloride, &c.

5:5′-Diamino-1:1′-arseno-2:2-stilbene:



contains an 8-membered ring consisting of six C and two As atoms (*Karrer*, B. 1915, **48**, 305). The corresponding arsinic acid is formed from 5-nitro-2-methyl-phenylarsinic acid by the action of caustic soda and subsequent reduction, and on further reduction with hyposulphite yields the ring compound.

An arsenic analogue of N-methyl piperidine is:



obtained by condensing dichloromethyl-arsine, $AsMeCl_2$, with the magnesium derivative of 1:5-dichloropentane and distilling the product (Bull. Soc. 1916 [iv], **19**, 151, 290). It is termed **1-methylarsepedine**, is a colourless liquid, b.-pt. 160°, with a strong smell of mustard, and is readily oxidized in contact with the air.

LIV. SYNTHETIC DRUGS

The earlier drugs of Pharmacology were all derived from organized structures, mainly of vegetable origin, and even at the present time extracts and tinctures of plant tissues are frequently prescribed. In many cases, however, the actual active principles present in such plant tissues have been isolated, and are now generally made use of in preference to the simple plant extracts. The advantages of such pure chemical compounds are numerous: other substances with quite different physiological properties are eliminated, and correct relationships between dose and physiological effect can be established. Many of these active principles belong to the groups of compounds known as alkaloids (p. 592) and glucosides (p. 646). The chemical study of these compounds has, in many cases, resulted in the elucidation of their structure, and subsequently led to their synthesis, *e.g.* atropine (p. 607), narcotine (p. 602), adrenaline (p. 899), cocaine (p. 608).

There is still, however, a number of well-known drugs of organic origin which have not been synthesised, and which are used in large quantities in medicine; well-known examples are the alkaloids, quinine and strychnine, and the glucosides of digitalis. The synthesis of quinine substitutes has been undertaken (J. C. S. 1929, 2945, 2965; 1930, 1256; J. Ind. 1930, 757) and **plasmoquine,** 8 (diethylaminoisopentylamino-6-methoxyquinoline is already on the market.

Not only have some of the active constituents of plants and animals been synthesised, but, in addition, numerous other synthetic products have been introduced into medicine to take the place of the older drugs. Hundreds of such compounds have been introduced: many have not received general recognition, but others have become as well known in medicine as the older drugs, *e.g.* phenacetin, aspirin, novocaine, &c. Many of these new synthetic drugs are manufactured from by-products obtained in the synthetic dye industry, and undoubtedly the two industries are interdependent on each other.

The world production of pharmaceuticals (including synthetics) in 1929 is estimated at £150,000,000, nearly double the value for 1913.

The syntheses of several well-known alkaloids have already

been given, and in this chapter the synthetic drugs are divided into the following groups:

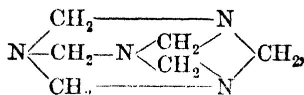
1. Antiseptics. 2. Hypnotics. 3. Antipyretics. 4. Diuretics and various. 5. Synthetic alkaloids and substitutes.

A. Antiseptics

1. FORMALDEHYDE GROUP

Formaldehyde, $CH_2\cdot O$ (p. 135) is a powerful antiseptic, and its vapour is used for disinfecting rooms. It cannot be used directly for internal use as it is highly corrosive and has toxic properties. Within recent years numerous condensation products of the aldehyde have been introduced into medicine, and most of these owe their activity to the fact that they slowly decompose in the organism, yielding formaldehyde. The most important of such derivatives are the colourless, odourless, non-irritant products formed by condensing the aldehyde with carbohydrates, and the best known of these is the condensation product with lactose known under the name of **formamint.**

The condensation product with ammonia, viz. hexamethylene-tetramine (p. 135), which is usually represented by a bridged ring structure:



is largely used in medicine under the names **Hexamine, Urotropine, Cystogen,** &c., as a urinary antiseptic. It has strong antiseptic properties, and its aqueous solution produces no irritant effects. Numerous derivatives of hexamine have also been introduced, both as antiseptics and as uric acid eliminants, mainly as additive compounds with substances such as camphoric acid, sodium acetate, sodium citrate, and sodium benzoate. **Tannoform,** a condensation product of formaldehyde and tannic acid, $CH_2(C_{14}H_9O_9)_2$, is used both as an antiseptic and as an astringent.

Dermatol, a derivative of gallic acid, viz. basic bismuth gallate, $C_6H_2(OH)_3\cdot COOBi(OH)_2$, is an iodoform substitute, as is also **airol,** a basic bismuth iodide gallate, $C_6H_2(OH)_3\cdot CO\cdot OBi(OH)I$.

2. PHENOLIC GROUP

Phenol (p. 440) is one of the common organic antiseptics, and many others are hydroxylated derivatives of benzene hydrocarbons. The cresols are more effective antiseptics than phenol and are less toxic, but suffer from the fact that they are less soluble in water. **Lysol** is a solution of cresols in soft soap.

Thymol (p. 446) is used as an antiseptic and also as a poison for intestinal parasites such as tapeworms, &c., but as a rule the carbonate, $CO[O\cdot C_6H_3(CH_3)C_3H_7]_2$, obtained by the action of carbonyl chloride on thymol, and known as **hymatol** is used. The polyhydric phenols are more toxic than phenol, and are made use of in treating skin diseases. The following derivative of β-naphthol, $OH\cdot C_{10}H_6\cdot \underset{1}{CH_2}\cdot C_6H_3(\underset{2}{O}H)COOH$, is used in dermatology under the name of **epicarine.**

The investigations of *Bechold* and *Ehrlich* (Zeit. physiol. 1906, **47,** 173) on the general properties of substituted phenols prove that the introduction of chlorine and bromine atoms into a phenol increases its antiseptic properties, *e.g.* *s*-tribromophenol (p. 443) is forty-six times as active as phenol, and brominated cresols are still more active. Most of these compounds, however, are too toxic for internal use. According to *R. von Walther* and *Zipper* (J. pr. Chem. 1915, **91,** 364), *p*-chloro-*m*-cresol, $OH\cdot C_6H_3Cl\cdot CH_3$ (1:4:3), prepared by the action of sulphuryl chloride on *m*-cresol, is superior as a disinfectant to all other analogous phenol derivatives, and is used in conjunction with sodium or potassium ricinoleate to increase its solubility. Picric acid is an excellent germicide.

The introduction of a 4-normal alkyl group into phenol, *m*-cresol or guaiacol increases their antiseptic properties and in all cases the *n*-amyl group has the maximum effect (J. Ind. 1930, 759).

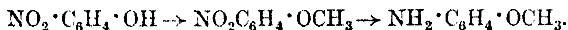
The introduction of a carboxylic group into the phenol molecule lowers both its toxic and antiseptic properties, and *o*-hydroxybenzoic acid, or salicylic acid, and its salts are common antiseptics (for synthesis cf. p. 487), as is also the phenyl ester of salicylic acid known as **salol,** $OH\cdot C_6H_4\cdot CO_2C_6H_5$ (p. 488). The chief use, however, for salicylic acid and its salts in medicine is for cases of acute rheumatism, when its action is most marked. As the acid and its salts produce gastric troubles,

they have been largely replaced by acetyl-salicylic acid, **aspirin,** $CH_3 \cdot CO \cdot O \cdot C_6H_4 \cdot COOH$, and its salts. The sodium salt is **tylnatrin** and the calcium **kalmopyrin.** The natural glucoside, salicin (p. 648), is sometimes administered, as in the organism it is hydrolysed to glucose and salicyl alcohol, which is slowly oxidized to salicylic acid.

Sodium cinnamate (*hetol*) has been recommended in cases of tuberculosis, in aqueous or better in glycerol solutions, and *m*-cresyl cinnamate, $C_6H_5 \cdot CH:CH \cdot COOC_6H_4 \cdot CH_3$, known as **hetocresol,** is used as a dusting powder for tuberculous wounds.

In the organism salol is hydrolysed very slowly to phenol and salicylic acid, and both of these exert their antiseptic properties. The method of synthesis of salol has been used for the preparation of numerous other esters derived from salicylic acid and also from other acids. Some of these esters can also be prepared by heating salol with another phenol, *e.g.* quinol, eugenol, carvacrol. **Monosalicylin,** $OH \cdot CH_2 \cdot CH(OH) \cdot CH_2 \cdot O \cdot CO \cdot C_6H_4 \cdot OH$, is known as *glycosal.* **Methyl acetylsalicylate,** $CH_3 \cdot CO \cdot O \cdot C_6H_4 \cdot COOCH_3$, is *methylrodin,* and **methyl benzoylsalicylate** is *benzosalin.* **β-Naphthyl salicylate,** which is next in importance to salol, is known as *betol* or *naphtholsalol,* **menthyl salicylate** is *salit,* and **phenyl salicylsalicylate** is *disalol.*

Guaiacol (p. 447) and its derivatives are also used for medicinal purposes. A common synthesis is from *o*-nitrophenol (p. 443), which is transformed into *o*-anisidine in the following stages:—



$$NO_2 \cdot C_6H_4 \cdot OH \rightarrow NO_2C_6H_4 \cdot OCH_3 \rightarrow NH_2 \cdot C_6H_4 \cdot OCH_3.$$

The anisidine is then diazotized, and the solution poured into a mixture of sulphuric acid and sodium sulphate at 135°–160°, when the guaiacol distils over. **Guaiacyl carbonate** or *duotal,* $(OCH_3 \cdot C_6H_4 \cdot O)_2CO$, made from the sodium derivative of guaiacol and carbonyl chloride, is less toxic than guaiacol. **Guaiacyl phosphite,** *phosphatol,* $P(O \cdot C_6H_4 \cdot OCH_3)_3$, from phosphorus trichloride and an alkaline solution of guaiacol, the benzoate, cinnamate, acetate, and cacodylate have all been prepared. The monoglyceryl ether, **guaiamar,** $OH \cdot CH_2 \cdot CH(OH) \cdot CH_2 \cdot O \cdot C_6H_4 \cdot OCH_3$, from monochlorhydrin (p. 200) and alkaline guaiacol, is soluble in water, and is hydrolysed to its components in the organism. **Potassium guaiacol-3-**

sulphonate, $OH \cdot C_6H_3(OCH_3)SO_3K$, known as *thiocoll,* is less irritant than guaiacol.

3. IODINE COMPOUNDS

Various iodine derivatives are used as antiseptics, the best known of which is the external antiseptic **iodoform,** CHI_3 (p. 66). A compound of iodoform with hexamethylenetetramine, known as **iodoformin,** is odourless, as is also the compound with hexamethylene-tetramine-ethyl-iodide known as **iodoformal.** Both compounds are decomposed by water into their components. *Iodol* or **tetraiodopyrrole** is odourless and non-irritant, and resembles iodoform in the fact that its action is probably due to the liberation of iodine. It is prepared by the action of iodine on an alkaline solution of pyrrole (p. 551).

Compounds of the type of *s*-triiodo-*m*-cresol prepared by the action of iodine on $C_6H_3(CH_3)(OH)CO_2H$ (1:3:4), or on *m*-cresol, resemble phenol in antiseptic properties. The iodoxyl compounds containing the group $\cdot OI$ have powerful antiseptic and anti-syphilitic properties, *e.g.* *aristol,* **dithymol diiodide,** $C_3H_7 \cdot C_6H_2Me(OI) \cdot C_6H_2Me(C_3H_7) \cdot OI$. Another type of iodine derivative is *p*-**iodoxy-toluene,** *isoform,* $CH_3 \cdot C_6H_4 \cdot IO_2$, valuable as a dry antiseptic.

4. CHLORAMINE GROUP

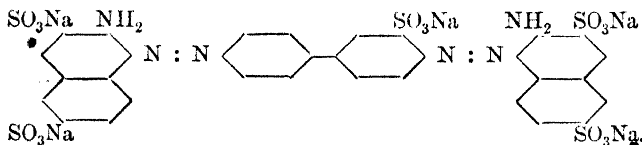
Recently organic chlorine derivatives containing chlorine attached to nitrogen have been introduced as disinfectants in the place of sodium hypochlorite. Their physiological action is similar to that of hypochlorite, but they are less irritant and much more stable, and it is easy to obtain aqueous solutions of definite strength. They are largely used for treatment of infected wounds. The compounds are generally known as **chloramines,** and are prepared by the action of hypochlorite solutions on compounds containing the NH or NH_2 groups. (Cf. *Chattaway*, J. C. S. 1905, **87,** 145). The commonest of these compounds is sodium *p*-toluenesulphonechloramide, $CH_3 \cdot C_6H_4 \cdot SO_2 \cdot NClNa, 3H_2O$, known generally as **chloramine T** or **tolamine.** It is made from *p*-toluenesulphonylchloride, $CH_3 \cdot C_6H_4 \cdot SO_2Cl$, a by-product in the manufacture of saccharine (p. 482). This is converted by the action of ammonia into the corresponding amide, which yields chloramine T when warmed with sodium hypochlorite solution.

The corresponding dichloro-derivative, ***dichloramine T***, made from *p*-toluenesulphonamide by the action of bleaching-powder, and the carboxylic acid, ***p*-sulphone-dichloraminobenzoic acid**, *halazone*, $CO_2H \cdot C_6H_4 \cdot SO_2 \cdot NCl_2$, prepared by oxidizing *p*-toluenesulphonamide with dichromate and sulphuric acid and treating an alkaline solution of the product with chlorine, are both good disinfectants. The latter is recommended for sterilizing drinking-water. (Compare *Dakin*, B. Med. J. 1917, 833.)

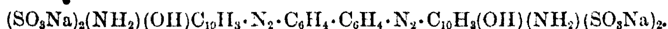
5. GROUP OF ANILINE DYES

Many aniline dyes have antiseptic properties, and several of these have found use in medicine, more particularly for destroying the protozoa characteristic of certain diseases. A few of the more important dyes used are:—

Trypan red, obtained by diazotizing both amino-groups in benzidineorthosulphonic acid, $NH_2 \cdot C_6H_4 \cdot C_6H_3(SO_3H) \cdot NH_2$, and coupling the diazonum salt with 2-naphthylamine-3:6-disulphonic acid. Its structural formula is:



Trypan blue is obtained by diazotizing *o*-tolidine (p. 506) and coupling the tetrazo-compound with 8-amino-1-naphthol-3:6-disulphonic acid, and has the formula:



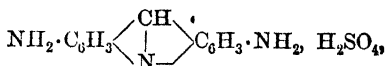
$$(SO_3Na)_2(NH_2)(OH)C_{10}H_3 \cdot N_2 \cdot C_6H_4 \cdot C_6H_4 \cdot N_2 \cdot C_{10}H_3(OH)(NH_2)(SO_3Na)_2.$$

Characteristic of the dyes of the benzidine series possessing trypanocidal properties is the presence of sulphonic acid groups in the 3:6 positions.

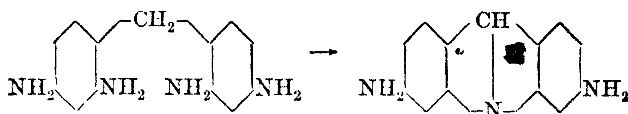
Brilliant green, the sulphate of the ethyl base corresponding with malachite green (p. 516), prepared from benzaldehyde, diethylaniline, sulphuric acid, and an oxidizing agent such as lead peroxide, has the structure $NEt_2 \cdot C_6H_4 \cdot C(C_6H_5):C_6H_4:NEt_2HSO_4$, and is largely used as a general antiseptic.

Methylene blue (p. 938) is used internally for various diseases, including rheumatism, nephritis, &c.

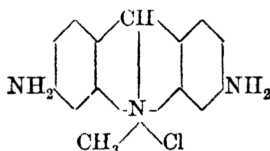
Proflavine, or 3:6-diamino-acridine-sulphate,



is prepared synthetically from *p-p*-diamino-diphenylmethane: this is nitrated, and then reduced with tin and hydrochloric acid, when 2:4:2':4'-tetra-amino-diphenylmethane is obtained. The solution containing the reduction product in the form of its stannichloride is heated in an autoclave at 140°, when ring formation occurs, ammonia is eliminated, and 3:6-diamino-acridine is obtained:



Acriflavine, 3:6-diaminomethylacridinium chloride,



is obtained by acetylating proflavine, methylating the tertiary nitrogen atom by means of methyl sulphate, and then eliminating the acetyl groups and heating with hydrochloric acid. These two acridine dyes have been recommended for the treatment of wounds; they are highly antiseptic and devoid of irritant or toxic action, and do not inhibit the process of healing.

Compare also P. Roy. S., 1926, **100**, 293; 1929, **105**, 99; Lancet, 1929, 968.

B. Hypnotics and Anæsthetics

The oldest of these is morphine, but it has now been largely replaced by synthetic materials which are free from the unpleasant and dangerous properties of morphia. General anæsthetics are closely related to hypnotics from a physiological standpoint, but are usually volatile compounds, which are

administered by inhalation, as their effects are then so much more rapid and the duration much more readily controlled.

The hypnotics and general anæsthetics belong to various groups of carbon compounds. General anæsthetics comprise the group of halogen derivatives of aliphatic hydrocarbons and the group containing alkyl, particularly ethyl, groups. The non-volatile narcotics include compounds of these types, and also many compounds containing the carbonyl group, and others contain a heterocyclic nitrogen ring.

Various attempts have been made to establish relationships between hypnotic action and physical properties. In many cases it is found that in a given series of hypnotics the physiological activity increases with the distribution coefficients of the substances for fat and water, or, in other words, with the rapidity of diffusion of the substance into protoplasm (*Overton*, *H. Meyer*). There are various substances, however, which have a high distribution coefficient, but are without hypnotic action. According to *Traube*, the osmotic permeability, or in other words the surface tension of the substance, determines the narcotic action. In reality both surface tension and the distribution coefficient are important physical factors affecting hypnotic action. *Baglioni* suggests that the narcotic action is due to deprivation of oxygen, and it has been shown that chloroform, ether, and chloral hydrate diminish the oxidizing capacity of tissues.

1. HALOGEN ANÆSTHETICS AND HYPNOTICS

The best-known halogen anæsthetic is chloroform (p. 66). Pure chloroform is unstable, and is decomposed by air and moisture, yielding phosgene, which is highly injurious. This decomposition is prevented by the addition of about 2 per cent of ethyl alcohol.

A German process for the manufacture of chloroform consists in saturating alcohol (95 per cent) with chlorine, and then allowing the chlorinated product to flow over calcium hydroxide mixed with a little bleaching-powder. The other halogen derivatives of methane also possess hypnotic action, which tends to increase with the amount of chlorine present, thus carbon tetrachloride is more effective than chloroform, but is not generally used, as it is more toxic. Ethyl chloride (p. 61) is used both as a general and a local anæsthetic, but

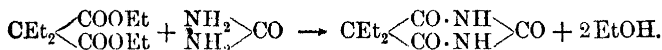
its use for the latter is simply due to the low temperature produced by its rapid evaporation. Chloral hydrate, which is non-volatile, is a common hypnotic; it cannot be injected subcutaneously, as it has a deleterious after-effect on the heart. Its activity is not due to the formation of chloroform, as trichloroethyl alcohol and not chloroform is formed in the system. Many compounds and derivatives of chloral are used, but all these depend on the primary liberation of chloral, and have few or no advantages over chloral hydrate. Chloralformamide, $CCl_3 \cdot CH(OH) \cdot NH \cdot CHO$ (*chloralamide*) is a mild hypnotic and sedative. **Dormiol,** $CCl_3 \cdot CH(OH) \cdot O \cdot CMe_2 \cdot CH_2 \cdot CH_3$, is a condensation product of chloral and tertiary amyl alcohol. Chloral urethane, $CCl_3 \cdot CH(OH) \cdot NH \cdot CO_2C_2H_5$, yields a soluble ethyl derivative known as **somnal.**

Tertiary trichlorobutyl alcohol, $CCl_3 \cdot C(CH_3)_2OH$, **chloretone,** obtained by condensing acetone and chloroform in the presence of potassium hydroxide, is a crystalline solid, m.-pt. 96°, and has no irritant action on the stomach, but acts as a sedative, and is used in cases of sea-sickness and vomiting. Bromal hydrate in large doses has an anæsthetic action. Various bromine derivatives act as mild hypnotics. Some of these are: **Bromopin,** a compound of bromine and sesamé oil which can be used as a substitute for potassium bromide; sodium α-bromoisovalerate, **valerobromine,** $CH(CH_3)_2 \cdot CHBr \cdot CO_2Na$; bornyl α-bromoisovalerate, $CH(CH_3)_2 \cdot CHBr \cdot CO_2C_{10}H_7$, **bromovalol** or **eubornyl,** and α-bromoiso-valerylurea, $CH(CH_3)_2 \cdot CHBr \cdot CO \cdot NH \cdot CO \cdot NH_2$, **bromurul** or **dormigene,** and also bromo-derivatives of protein, *e.g.* **bromoglydine** and **bromalbin.** Analogous iodine compounds are also used, *e.g.* **iodipin,** analogous to bromopin, **iodival,** or iodoisovalerylurea, and iodo-derivatives of proteins; most of these compounds are used as substitutes for alkali iodides which often produce unpleasant symptoms.

2. ETHYL ANÆSTHETICS

A second important group of anæsthetics comprises the compounds containing alkyl groups attached to OH or O. Methyl groups appear to be inactive, but compounds containing ethyl, and especially tertiary alkyl groups, *e.g.* $\cdot CMe_3$, $\cdot CMe_2Et$, and CEt_3 have strong hypnotic action. Ethyl alcohol is useless, as very large doses are required to produce

sleep, probably owing to the readiness with which it is oxidized in the tissues. Ethyl ether is a very common anæsthetic. The higher alcohols are not employed, as they are not readily volatile. Derivatives of urea containing a tertiary alkyl group are also efficient hypnotics, tertiary-amyl-urea, $NH_2 \cdot CO \cdot NH \cdot CMe_2Et$, being one of the best. Certain ureides are also used. Diethylmalonylurea or diethylbarbituric acid is the well-known **veronal** (p. 298); the activity of the corresponding dipropyl compound is so intense that it is too dangerous for general use. These dialkylated barbituric acids can be prepared by condensing dialkylmalonic esters with urea in the presence of sodium ethoxide:



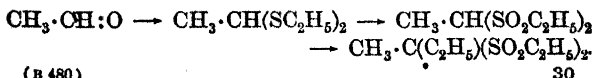
$$CEt_2<^{COOEt}_{COOEt} + ^{NH_2}_{NH_2}>CO \longrightarrow CEt_2<^{CO \cdot NH}_{CO \cdot NH}>CO + 2\,EtOH.$$

Many of the urethanes (p. 291) exhibit hypnotic properties, the best known of these is **hedonal**, methylpropylcarbinyl urethane, $NH_2 \cdot CO \cdot OCH(CH_3)C_3H_7$, prepared by the action of urea nitrate on methylpropylcarbinol.

Most ketones can act as hypnotics. Those containing ethyl groups are more active than those containing methyl; the true aromatic ketones have only a mild action, but mixed ketones, *e.g.* acetophenone, **hypnone**, $C_6H_5 \cdot CO \cdot CH_3$, and phenyl ethyl ketone, $C_6H_5 \cdot CO \cdot C_2H_5$, are much more active.

3. SULPHONES

A group of great practical importance are the sulphone derivatives, the most important representatives of which are **sulphonal**, $C(CH_3)_2(SO_2C_2H_5)_2$, and **trional**, $CH_3 \cdot C(C_2H_5)(SO_2C_2H_5)_2$. Sulphonal is manufactured by condensing acetone and ethyl mercaptan in the presence of zinc chloride and oxidizing the resulting mercaptol with excess of permanganate (p. 143). Trional can be prepared in a similar manner by replacing acetone by methyl ethyl ketone, and using hydrogen chloride as a condensing agent. An alternative method is to condense acetaldehyde with ethyl mercaptan, oxidize the mercaptol, and then ethylate with ethyl iodide and alkali:

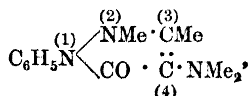


$$CH_3 \cdot CH{:}O \longrightarrow CH_3 \cdot CH(SC_2H_5)_2 \longrightarrow CH_3 \cdot CH(SO_2C_2H_5)_2 \longrightarrow CH_3 \cdot C(C_2H_5)(SO_2C_2H_5)_2.$$

Baumann and *Kast* (Zeit. physiol. 1890, **14,** 52) have investigated the relationship between the constitution and physiological activity of sulphone derivatives. The compounds, $CH_2(SO_2CH_3)_2$, $CH_2(SO_2C_2H_5)_2$, $SO_2C_2H_5 \cdot CH_2 \cdot CH_2 \cdot SO_2C_2H_5$, are inactive, also $CH_3 \cdot CH(SO_2CH_3)_2$, whereas $CH_3 \cdot CH(SO_2C_2H_5)_2$, ethylidene diethylsulphone and $C(C_2H_5)_2(SO_2CH_3)_2$ have activities comparable with that of sulphonal.

C. Antipyretics

Quinine is able to reduce the body temperature in cases of fever, *i.e.* it is an antipyretic, but at the same time it has a specific effect against malaria. The first synthetic experiments were made with the object of obtaining substances comparable with quinine, which was known to be a quinoline derivative, although its structure was not then established. Various alkylated tetrahydroquinolines were prepared and shown to possess antipyretic action; **kairine,** 1-ethyl-5-hydroxytetrahydroquinoline is one of the most effective, but all these compounds are useless as they are toxic to red blood corpuscles. *Knorr* was the first to produce a valuable synthetic antipyretic in 1887 in the substance known as **antipyrine** (p. 563). This compound has greater antipyretic activity than quinine, but has no specific action against malaria. Like many of the synthetic antipyretics it has a powerful analgesic action, *i.e.* it can act on the nervous system and soothe pain, especially neuralgic pain. Numerous derivatives have been put on the market, but most of these are not superior to the original antipyrine. A valuable derivative is **pyramidone,** 4-dimethylamino-antipyrine:



which is prepared by the following process from antipyrine: nitrous acid yields the 4-nitroso derivative, and this is readily reduced to the corresponding amine, which when methylated yields pyramidone.

The cheapest of all antipyretics is acetanilide (**antefebrine**) (p. 410). It has valuable antipyretic and analgesic properties,

but suffers from the defect that aniline is gradually liberated in the system, and symptoms of aniline poisoning may become apparent. Various other anilides have been suggested for use but have met with little favour.

Phenylurethane, $C_6H_5 \cdot NH \cdot CO_2C_2H_5$ (**euphorin**), from ethyl chloroformate and aniline, has marked analgesic properties.

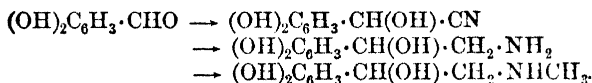
Phenacetin, *p*-ethoxyacetanilide, $OC_2H_5 \cdot C_6H_4 \cdot NH \cdot CO \cdot CH_3$ (p. 444), is the best-known representative of the *p*-aminophenol derivatives, and the corresponding methoxy derivative is even more active, but is also more toxic. The propyl and butyl ethers are much less active. The idea that derivatives of *p*-aminophenol might be useful as drugs was suggested by the observation that this is the main product formed when aniline and its simple derivatives are introduced into the organism. Numerous derivatives of phenacetin have been tried but none has any advantage; in all cases the therapeutic effect appears to be due to the liberation of *p*-aminophenol or of its ethyl ether in the tissues. The ethyl derivative, $OEt \cdot C_6H_4 \cdot NEt \cdot CO \cdot CH_3$, is even more efficient than phenacetin, but its higher cost militates against its use. Numerous compounds in which the acetyl group of phenacetin is replaced by other acyl groups, *e.g.* lactyl, diacetyl, salicyl, mandelyl, have been examined but are not so effective as the acetyl compound. Various condensation products of phenetidine, $OC_2H_5 \cdot C_6H_4 \cdot NH_2$, with aldehydes have been prepared, *e.g.* with salicylaldehyde, vanillin, and vanillin ethyl carbonate. Amino-phenacetin, **penocoll,** $OEt \cdot C_6H_4 \cdot NH \cdot CO \cdot CH_2 \cdot NH_2$, prepared from ammonia and bromoacetylphenetidine, is similar in action to phenacetin, it has a greater analgesic action, and is a good substitute for salicylic acid in cases of rheumatic fever.

A very common drug is acetylsalicylic acid, $CH_3 \cdot CO \cdot O \cdot C_6H_4 \cdot CO_2H$, **aspirin,** and is made by the action of acetyl chloride and zinc chloride, or of sodium acetate and acetic anhydride on the acid. Salicylosalicylic acid, **diplosal,** $OH \cdot C_6H_4 \cdot CO \cdot O \cdot C_6H_4 \cdot CO_2H$, and succinylsalicylic acid, **diaspirin,** are also used.

Derivatives of Ethylamine.—Drugs with sympathomimetic action, *i.e.* drugs which stimulate the sympathetic nervous system and produce rise in blood pressure.

The most important of these is *l*-**adrenaline,** 3:4-$(OH)_2C_6H_3 \cdot$

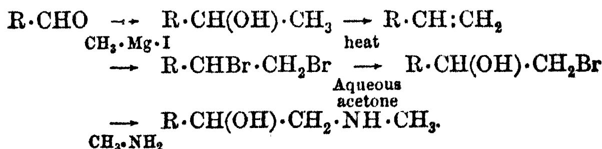
$CH(OH)\cdot CH_2\cdot NH\cdot CH_3$, a crystalline compound obtained from the suprarenal glands (*Takamine*, Am. J. Pharm. 1901, **73**, 523; for constitution compare *Jowett*, J. C. S. 1904, **85**, 192). The constitution is confirmed by the fact that the oxidation product known as adrenalone is identical with the synthetic compound derived from methylamine and chloroacetylcatechol, and must be represented as $(OH)_2C_6H_3\cdot CO\cdot CH_2\cdot NH\cdot CH_3$ (*Friedmann*). Adrenaline is formed when the sulphate of the amino-ketone is reduced with aluminium amalgam or electrolytically. An interesting synthesis (Jap. Pats. 1918) is from protocatechuic aldehyde: this is converted into the diacetyl derivative, which condenses with nitromethane in feebly alkaline solution, giving β-hydroxy:β-3:4-diacetoxyphenylnitroethane $(OAc)_2C_6H_3\cdot CH(OH)\cdot CH_2\cdot NO_2$; when this is mixed with formaldehyde and reduced with zinc and acetic acid, the diacetyl derivative of adrenaline $(OAc)_2C_6H_3\cdot CH(OH)\cdot CH_2\cdot NHMe$ is formed, and this on hydrolysis gives adrenaline. *r*-Adrenaline can also be prepared by condensing protocatechuic aldehyde with hydrogen cyanide, reducing the resulting nitrile to the primary amine, which is then methylated,



$$
\begin{aligned}
(OH)_2C_6H_3\cdot CHO &\rightarrow (OH)_2C_6H_3\cdot CH(OH)\cdot CN \\
&\rightarrow (OH)_2C_6H_3\cdot CH(OH)\cdot CH_2\cdot NH_2 \\
&\rightarrow (OH)_2C_6H_3\cdot CH(OH)\cdot CH_2\cdot NHCH_3.
\end{aligned}
$$

The racemic compound can be resolved by means of *d*-tartaric acid and also by means of *Penicillium glaucum*. This method is not used commercially. It is interesting to note that the *l*-compound is about twelve times as active physiologically as the corresponding *d*-compound.

The methylene and dimethyl ethers of adrenaline have also been synthesised, *e.g.* the dimethyl from veratraldehyde and the methylene ether from piperonal (p. 458), as denoted by the following scheme, where R represents either the $(OMe)_2C_6H_3$ or $CH_2O_2C_6H_3$ groups:



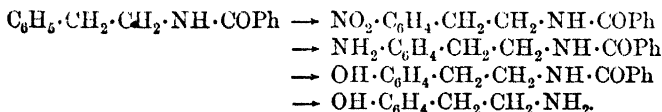
$$
\begin{aligned}
R\cdot CHO &\xrightarrow[CH_3\cdot Mg\cdot I]{} R\cdot CH(OH)\cdot CH_3 \xrightarrow[\text{heat}]{} R\cdot CH:CH_2 \\
&\rightarrow R\cdot CHBr\cdot CH_2Br \xrightarrow[\text{Aqueous acetone}]{} R\cdot CH(OH)\cdot CH_2Br \\
&\xrightarrow[CH_3\cdot NH_2]{} R\cdot CH(OH)\cdot CH_2\cdot NH\cdot CH_3.
\end{aligned}
$$

Adrenaline is largely used in conjunction with the local anæsthetics cocaine and eucaine, as it tends to check bleeding; it is also used to neutralize the toxic effects of cocaine, and is used as a specific for hay fever.

The parent substance of the group of adrenaline derivatives, viz. parahydroxyphenylethylamine, **tyramine,** $OH \cdot C_6H_4 \cdot CH_2 \cdot CH_2 \cdot NH_2$, can be obtained by elimination of carbon dioxide from tyrosine (p. 489 and 787), $OH \cdot C_6H_4 \cdot CH_2 \cdot CH(CO_2H) \cdot NH_2$; it is present in putrid meat, and is undoubtedly derived from the tyrosine present in the meat, just as phenylethylamine and isoamylamine, which are also present in putrid meat, are derived from the corresponding carboxylic derivatives, phenylalanine (pp. 483 and 787), and leucine (p. 224). Parahydroxyphenylethylamine is also present in the aqueous extract of the drug ergot, and its synthesis has led to its therapeutic use. The following synthetical methods have been adopted:

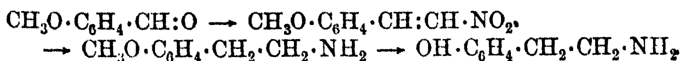
1. *p*-Hydroxybenzyl cyanide on reduction with sodium and alcohol yields the amine (*Barger*, J. C. S. 1909, **95,** 1123).

2. Phenylethylamine from benzylcyanide is benzoylated and then nitrated, the nitro compound is reduced to the corresponding amine, and this, by means of nitrous acid, transformed into the hydroxy derivative, and finally the benzoyl group is removed by hydrolysis (*Barger* and *Walpole*, ibid. 1720).



$$C_6H_5 \cdot CH_2 \cdot CH_2 \cdot NH \cdot COPh \rightarrow NO_2 \cdot C_6H_4 \cdot CH_2 \cdot CH_2 \cdot NH \cdot COPh$$
$$\rightarrow NH_2 \cdot C_6H_4 \cdot CH_2 \cdot CH_2 \cdot NH \cdot COPh$$
$$\rightarrow OH \cdot C_6H_4 \cdot CH_2 \cdot CH_2 \cdot NH \cdot COPh$$
$$\rightarrow OH \cdot C_6H_4 \cdot CH_2 \cdot CH_2 \cdot NH_2.$$

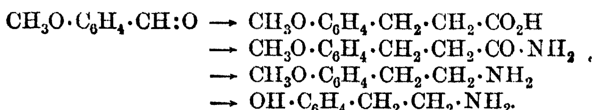
3. Anisaldehyde and nitromethane react in the presence of dilute alkali, yielding β-nitro-*p*-methoxycinnamene; this is reduced to the corresponding saturated amine, and the methyl ether converted into the free phenol by means of hydriodic acid (*Rosenmund*, B. 1909, **42,** 4778):



$$CH_3O \cdot C_6H_4 \cdot CH{:}O \rightarrow CH_3O \cdot C_6H_4 \cdot CH{:}CH \cdot NO_2$$
$$\rightarrow CH_3O \cdot C_6H_4 \cdot CH_2 \cdot CH_2 \cdot NH_2 \rightarrow OH \cdot C_6H_4 \cdot CH_2 \cdot CH_2 \cdot NH_2$$

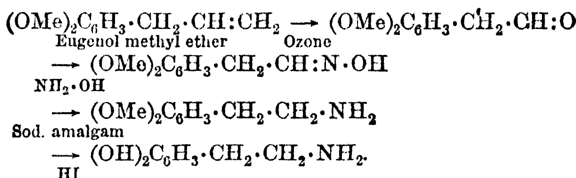
4. Starting with anisaldehyde, *p*-methoxycinnamic acid is prepared by condensing with ethyl acetate in the presence of finely-divided sodium. This acid is reduced to the corre-

sponding saturated acid, which is converted into its chloride and then into the amide, which, by the *Hofmann* reaction, yields the amine. The last stage consists in converting the methoxy into the hydroxy group by means of concentrated hydrobromic acid:

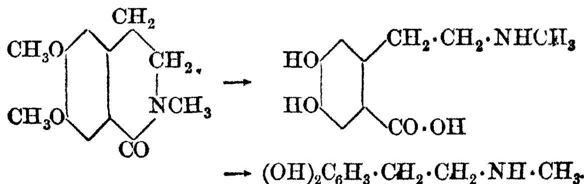


A number of compounds analogous to adrenaline but minus the hydroxyl of the secondary alcoholic group have been synthesised. The three following syntheses are typical:—

1. 3:4-dihydroxyphenylethylamine, $(OH)_2 \cdot C_6H_3 \cdot CH_2 \cdot CH_2 \cdot NH_2$ (*Mannich* and *Jacobsohn*, B. 1910, **43**, 189):

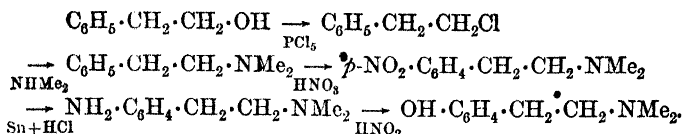


2. 3:4-dihydroxyphenylethyl-methylamine, $(OH)_2C_6H_3 \cdot CH_2 \cdot CH_2 \cdot NH \cdot CH_3$ (*Pyman*, J. C. S. 1910, **97**, 264), from 1-keto-6:7-dimethoxy-2-methyl-tetrahydroquinoline and hydrochloric acid at 170°–175°:



The methyl groups are removed, the ring is broken between the carbonyl group and nitrogen atom by the addition of water, and finally carbon dioxide is eliminated.

3. **Hordenine,** *p*-hydroxyphenylethyl-dimethylamine, a substance present in germinating barley, from phenylethyl alcohol (*Barger*, J. C. S. 1909, **95**, 2193):



$$C_6H_5\cdot CH_2\cdot CH_2\cdot OH \underset{PCl_5}{\longrightarrow} C_6H_5\cdot CH_2\cdot CH_2Cl$$

$$\underset{NHMe_2}{\longrightarrow} C_6H_5\cdot CH_2\cdot CH_2\cdot NMe_2 \underset{HNO_3}{\longrightarrow} p\text{-}NO_2\cdot C_6H_4\cdot CH_2\cdot CH_2\cdot NMe_2$$

$$\underset{Sn+HCl}{\longrightarrow} NH_2\cdot C_6H_4\cdot CH_2\cdot CH_2\cdot NMe_2 \underset{HNO_2}{\longrightarrow} OH\cdot C_6H_4\cdot CH_2\cdot CH_2\cdot NMe_2.$$

Hordenine is now made by methylating *p*-hydroxyphenylethylamine with methyl chloride.

Barger and *Dale* (J. physiol. 1910, **41,** 19) have made a careful comparison of the physiological properties of these and numerous similar compounds. Some of the conclusions they arrive at are:

1. The sympathomimetic action is characteristic of a large series of amines, the simplest being the primary aliphatic amines.

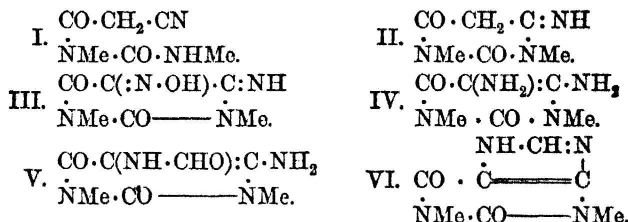
2. As the structure of the amine approaches that of adrenaline the activity increases. The optimum effect is attained with a carbon skeleton consisting of a benzene ring with a side chain of two carbon atoms, the terminal one bearing the amino group. Another condition for optimum effects is the presence of two phenolic hydroxyl groups in the positions 3:4-relative to the side chain. When these are present an alcoholic hydroxyl still further intensifies the activity. A phenolic hydroxyl in position 2 has no effect.

3. The quaternary ammonium salts corresponding with the amines related to adrenaline and tyramine have an action similar to that of nicotine.

D. Diuretics and Uric Acid Eliminants and Various Drugs

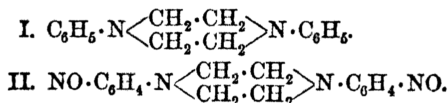
Most purine derivatives have diuretic action. The best known of these is caffeine, which is obtained from natural sources (p. 303), but its use in medicine is largely as a cerebral stimulant and a cardiac tonic in conjunction with other drugs, *e.g.* aspirin. The most powerful diuretic of the group is theophylline, 1:3-dimethylxanthine (p. 303), and is manufactured by *Traube's* synthetical method (B. 1900, **33,** 3053). Dimethylcarbamide and cyanoacetic acid condense in the presence of phosphorus oxychloride yielding (I), which is transformed by alkali into the cyclic base (II). This base yields an isonitroso compound (III), which can be reduced to the corresponding

diamine (IV) by means of ammonium sulphide. The diamine with formic acid yields a formyl derivative (V), which gives theophylline (VI) when heated with alkali.



Numerous remedies for gout have been suggested; these are either recommended with the idea of preventing the formation of uric acid or of dissolving it when formed and eliminating it from the system. Compounds of the first type are relatively complex acids, *e.g.* quinic acid from coffee beans (p. 491), diphenyl tartrate, hippuric acid (p. 476), salicylic acid derivatives.

Of uric acid solvents, **piperazine**, the reduction product of pyrazine (p. 590), was first obtained by *Hofmann* by the action of ammonia on ethylene dichloride or dibromide, and is most readily purified by means of its di-nitroso derivative, which yields the base when treated with hydrochloric acid or reducing agents. Another method is from ethylene dibromide and aniline. The product is diphenyl-piperazine (I); this with nitrous acid yields a nitroso derivative (II), which is hydrolysed by caustic soda to piperazine and *p*-nitrosophenol.



Various salts of piperazine are also used, *e.g.* piperazine quinate is **urol** or **sidonal**, and the tartrate of dimethylpiperazine is **lysetol.** The compound, $\begin{matrix}CH_2\cdot N= \\ CH_2\cdot NH\end{matrix}\!\!>C\cdot CH_3$, **lysidine,** has a solvent action eight times as great as that of piperazine.

Numerous hexamethylenetetramine derivatives have also been recommended as uric acid eliminants.

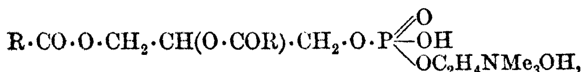
PURGATIVES

Many of the milder natural purgatives, such as cascara, senna, aloes, and rhubarb, appear to contain hydroxy derivatives of anthraquinone (p. 541) as their active constituents, and a number of synthetic hydroxy derivatives of anthraquinone have been investigated. Of these the most active is anthrapurpurin or the 1:2:7-trihydroxy derivative.

Certain derivatives of aloin, the active principle of aloes, have been prepared and used, *e.g.* the condensation product of aloin with formaldehyde and tribromoaloin and triacetylaloin.

GLYCEROPHOSPHATES

These compounds are of interest from their relationship to one of the chief constituents of nervous tissue and egg yolk, viz. lecithins. These are triglycerides, containing two complex acyl groups, such as those derived from stearic, palmitic, oleic, and other acids, and the third hydrogen is replaced by a choline-phosphoric acid group (p. 203), *e.g.*



$$R\cdot CO\cdot O\cdot CH_2\cdot CH(O\cdot COR)\cdot CH_2\cdot O\cdot P\begin{cases}=O\\ -OH\\ -OC_2H_4NMe_3OH,\end{cases}$$

where R represents a complex alphyl group such as $C_{17}H_{35}$.

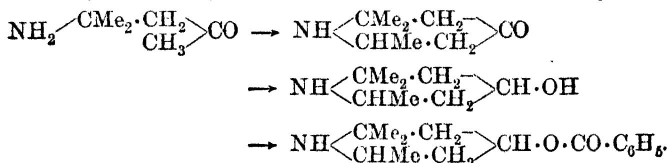
Synthetic sodium glycerophosphates have been introduced as nerve tonics; the monosodium salt, $ONa\cdot PO[OC_3H_5(OH)_2]_2$, can be prepared from monosodium phosphate and glycerol (2 mols.) by heating under reduced pressure, and if this is saponified with caustic soda the β-disodium glycerophosphate, $OH\cdot CH_2\cdot CH[O\cdot PO(ONa)_2]\cdot CH_2\cdot OH$, is formed.

E. Synthetic Alkaloids

(*a*) Attention has already (p. 599) been drawn to the various esters of quinine which are used instead of the natural alkaloid, as they are free from the bitter taste of the latter. These esters are much more expensive than quinine, and are not so generally used. The absence of bitter taste is largely due to their insolubility, and in the organism they are hydrolysed to quinine and the corresponding acid. Euquinine is manufactured by the action of ethyl chloroformate, $Cl\cdot CO_2C_2H_5$, on quinine.

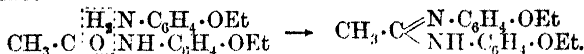
(*b*) *Synthetic tropeïnes.*—**Homatropine** (p. 607), the tropine ester of mandelic acid, $C_6H_5 \cdot CH(OH) \cdot CO \cdot OC_8H_{14}N$, is prepared on the large scale from its components, and is used as a substitute for atropine, as it is less toxic and its myriadic action develops and passes off more readily.

(*c*) *Cocaine substitutes.*—A synthetic local anæsthetic which has come into general use is **β-eucaine**, benzoylvinyl-diacetone-alkamine hydrochloride, $NH\langle{}^{CMe_2 \cdot CH_2}_{CHMe \cdot CH_2}\rangle CH \cdot O \cdot CO \cdot C_6H_5$ (*Harries*, B. 1896, **29**, 2730; A. 1897, **294**, 372; **296**, 328; 1898, **299**, 346). It can be synthesised by the following series of reactions: Acetone and ammonia yield diacetonamine (p. 141), which condenses with aldehyde, yielding the cyclic vinyldiacetonamine; this can be reduced to the corresponding secondary alcohol by sodium amalgam, and then benzoylated:



$$NH_2 \cdot CMe_2 \cdot CH_2 \cdot CO \cdot CH_3 \rightarrow NH\langle{}^{CMe_2 \cdot CH_2}_{CHMe \cdot CH_2}\rangle CO$$
$$\rightarrow NH\langle{}^{CMe_2 \cdot CH_2}_{CHMe \cdot CH_2}\rangle CH \cdot OH$$
$$\rightarrow NH\langle{}^{CMe_2 \cdot CH_2}_{CHMe \cdot CH_2}\rangle CH \cdot O \cdot CO \cdot C_6H_5.$$

Holocaine, the hydrochloride of $CH_3 \cdot C\langle{}^{N \cdot C_6H_4 \cdot OEt}_{NH \cdot C_6H_4 \cdot OEt}$, is used in ophthalmic surgery, and is manufactured by condensing phenetidine (p. 444) with its acetyl derivative phenacetine:



$$CH_3 \cdot C{}^{\vdots}_{O} \; {}^{H_2N \cdot C_6H_4 \cdot OEt}_{NH \cdot C_6H_4 \cdot OEt} \rightarrow CH_3 \cdot C\langle{}^{N \cdot C_6H_4 \cdot OEt}_{NH \cdot C_6H_4 \cdot OEt}.$$

It is sparingly soluble, and its solutions keep well, but it has toxic properties.

Stovaine, methyl-ethyl-dimethylaminomethyl-carbinyl benzoate, $C_6H_5 \cdot CO \cdot O \cdot CMeEt \cdot CH_2 \cdot NMe_2$, HCl, is a well-known anæsthetic, and is a representative of the group of compounds known as alkamine esters, which contain the grouping R·CO·O·C·C·NR. It is synthesised by the action of magnesium ethyl bromide on dimethyl-amino-acetone and benzoylation of the product

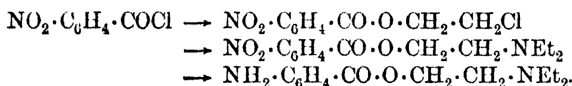


$$CH_3 \cdot CO \cdot CH_2 \cdot NMe_2 \rightarrow OH \cdot CMeEt \cdot CH_2 \cdot NMe_2.$$

Alypine is the corresponding tetramethyldiamino-di-methyl-ethyl-carbinyl benzoate, $C_6H_5 \cdot CO \cdot O \cdot CEt(CH_2NMe_2)_2$.

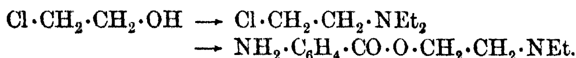
Numerous derivatives of amino- and hydroxyamino-benzoic acids have been introduced: the diethylglycine derivative of methyl 2-hydroxy-5-aminobenzoate, $NMe_2 \cdot CH_2 \cdot CO \cdot NH \cdot C_6H_3(OH) \cdot CO_2Me$, is **nirvanine**; ethyl *p*-aminobenzoate is **anæsthesine,** and its salt with *p*-phenolsulphonic acid is used for hypodermic injections under the name **subcutin. Novocaine,** the hydrochloride of diethylaminoethyl *p*-aminobenzoate, $NH_2 \cdot C_6H_4 \cdot CO \cdot O \cdot CH_2 \cdot CH_2 \cdot NEt_2$, HCl, is the most widely used of all local anæsthetics, as it is non-irritant, and only about one-seventh as toxic as cocaine. The following synthetic methods are used for its preparation:—

1. Condensation of *p*-nitrobenzoyl chloride with ethylene chlorhydrin, heating the product with diethylamine at 100°–120°, and reducing the nitro group by means of tin and hydrochloric acid:



$$\begin{aligned} NO_2 \cdot C_6H_4 \cdot COCl &\rightarrow NO_2 \cdot C_6H_4 \cdot CO \cdot O \cdot CH_2 \cdot CH_2Cl \\ &\rightarrow NO_2 \cdot C_6H_4 \cdot CO \cdot O \cdot CH_2 \cdot CH_2 \cdot NEt_2 \\ &\rightarrow NH_2 \cdot C_6H_4 \cdot CO \cdot O \cdot CH_2 \cdot CH_2 \cdot NEt_2. \end{aligned}$$

2. Ethylene chlorhydrin and diethylamine are condensed to form chlorethyldiethylamine, which is then heated with sodium *p*-aminobenzoate:



$$\begin{aligned} Cl \cdot CH_2 \cdot CH_2 \cdot OH &\rightarrow Cl \cdot CH_2 \cdot CH_2 \cdot NEt_2 \\ &\rightarrow NH_2 \cdot C_6H_4 \cdot CO \cdot O \cdot CH_2 \cdot CH_2 \cdot NEt. \end{aligned}$$

3. *p*-Aminobenzoic acid is condensed with ethylene chlorhydrin at 100° in sulphuric acid solution, and the product then heated with diethylamine at 100°–110°, or alternatively *β*-bromoethyl *p*-nitrobenzoate is synthesised from sodium *p*-nitrobenzoate and ethylene bromide, and this is then condensed with diethylamine and the nitro group in the resulting product reduced.

MORPHINE ALKALOIDS

Morphine has not been prepared synthetically, but numerous synthetic products have been obtained from it (cf. p. 605).

F. Constitution and Physiological Activity

The production of a large number of new synthetic drugs has led to the study of the relationship between chemical constitution and physiological action or therapeutic effect.

Numerous generalizations have been drawn, but, as a rule, these only hold within very narrow limits, and it may be stated that, on the whole, the relationships between chemical constitution and physiological activity still remain obscure.

The introduction of a sulphonic acid group into the molecule of a physiologically active substance usually reduces the activity; thus the sodium salts of phenolsulphonic acid and morphine-sulphonic acid are devoid of the activity characteristic of the parent substances. A carboxyl group has much the same effect, but if the carboxyl group is esterified the product frequently regains its toxic properties. The acetyl group often produces a diminution in toxic properties, as shown by a comparison of aniline and acetanilide.

An increase in toxicity and physiological activity is frequently produced by reducing a cyclic system containing nitrogen, as shown by a comparison of pyrrole, pyridine, and β-naphthylamine with pyrrolidine, piperidine, and tetrahydro-β-naphthylamine.

Nearly all amines, including alkaloids, when converted into quaternary ammonium salts lose their characteristic physiological effects, and become strong paralysers of motor nerve endings. Similar physiological effects are produced by phosphonium, arsonium, and sulphonium salts. An increase in the number of olefine linkings frequently produces marked physiological effects. This is shown by a comparison of allyl with propyl alcohol and of carvone (p. 624) with the saturated analogue menthone. In both cases the unsaturated compound has greater physiological activity.

The introduction of hydroxyl groups into the benzene ring increases the activity, whereas in the aliphatic series the introduction of such groups diminishes activity, as shown by a comparison of the inert sugars with the toxic simple aldehydes.

The alphyl nitrites tend to produce a dilatation of the blood-vessels or to lower the blood pressure. This property is most marked with amyl nitrite and least with the methyl compound. A similar property is characteristic of certain nitrates, particularly glyceryl trinitrate and erythryl tetranitrate, which are largely used in medicine. The aliphatic nitro-compounds, which are isomeric with the nitrites, are strong poisons and do not reduce blood pressure.

Optical isomerides do not necessarily possess the same

degree of physiological activity; thus atropine is intermediate in activity between the *d*- and *l*-hyoscyamines, which exhibit markedly different properties; *l*-nicotine is twice as poisonous as *d*-nicotine, and the two asparagines (p. 258) have different tastes.

The fate of drugs in the organism has received much attention. As a rule substances which are extremely readily decomposed, or substances which pass through the system quite unaltered, are of little value as drugs. The main changes which occur in the organism are (*a*) hydrolysis, (*b*) oxidation, (*c*) reduction. Hydrolysis can be due to the slightly acid stomach juices containing pepsin, or, in the case of esters, to the slightly alkaline juices of the small intestine, which contain the pancreatic enzyme trypsin. One of the objects of synthesising new products is to obtain substances which can pass the stomach without undergoing hydrolysis, but which are readily hydrolysed in the small intestine, yielding products which can then exert their specific action.

Oxidation frequently takes place, more particularly in the tissues or blood. Many aliphatic compounds are oxidized to carbon dioxide, water, and urea; others to acids. Many aliphatic compounds containing methyl groups or halogen are not readily oxidized. With aromatic compounds containing side chains the side chain is usually oxidized, but the benzene ring left intact. Compounds of the type $C_6H_5 \cdot CH_2 \cdot CH(NH_2) \cdot CO_2H$ are completely oxidized. Another type of oxidation is the formation of phenolic hydroxy groups, *e.g.* aniline yields *p*-aminophenol. Reduction also takes place in the blood and tissues, but is not so common as oxidation. Nitrobenzaldehydes can give rise to aminobenzoic acids and picric acid to dinitroamino-phenol.

As a rule the primary products of change, if they are toxic, are not excreted as such, but in the form of compounds with sulphuric acid or glycuronic acid, $CHO \cdot (CH \cdot OH)_4 \cdot CO_2H$. Thus phenol always forms sodium phenyl sulphate, $SO_2(ONa)OPh$, a non-toxic substance. Salicylic and benzoic acids are partly eliminated in the form of derivatives with glycine, *i.e.* in the form of compounds of the hippuric acid type.

LV. SYNTHETIC DYES

Before *Perkin's* synthesis of the first aniline dye in 1856, the dyestuffs used in dye-houses belonged to the group of natural colours, and were prepared from vegetable and animal tissues, *e.g.* alizarin from madder, fustic from the sumach tree, cochineal from the cochineal insect, *Coccus cacti*, and lac dye as a by-product in the manufacture of lac from the lac insect, *Coccus lacca*. At the present time nine-tenths of the dyes used in the cotton, woollen, and other industries are of synthetic origin, and are derived from coal-tar. A few natural dyes are still used; the most important of these are the logwood dyes, used for blacks on animal fibres and substances of the type of anatto and turmeric, which are used for colouring foodstuffs. In two cases severe competition has occurred between the natural dye and the same dye produced synthetically; in the one case, alizarin, the synthetic product has completely replaced the natural dye; in the other, indigo, the natural product has become [illegible] to such an extent that the area under cultivation has diminished enormously.

The number of artificial dyes is very large: in 1914 Germany produced about 900 different types of dyes, and new ones are continually being added. Some of the simpler of these, such as azo dyes, triphenylmethane dyes, and alizarin have been referred to in earlier chapters.

The extent of the synthetic dye industry can be gathered from the fact that in 1912 Germany produced dyestuffs to the value of £12,500,000, and that in the same year England used dyes to the value of £2,000,000, 90 per cent of which were imported. It is claimed that the United States of America in 1918 produced dyestuffs to meet all her demands, and in addition a quantity for export equivalent to £2,000,000. The war also gave a stimulus to the manufacture of dyes in England, France, Italy, and Japan; thus in 1917 Japan produced about 9,000,000 lb. of dyes.

The total value of synthetic dyes manufactured in 1927 is estimated at £35,000,000, and in 1929 Germany exported dyes to the value of £11,000,000, and in the same year England produced about 90 per cent of the dyes required for use in this country.

The more important synthetic dyestuffs can be classified as follows:—

A. Nitroso- and nitro-dyestuffs.
B. Azo-dyes.
C. Stilbene, pyrazole, and thiazole dyestuffs.
D. Di- and tri-phenylmethane dyes.
E. Xanthene dyestuffs.
F. Acridine and Quinoline dyestuffs.
G. Indamine and Indophenol dyestuffs.
H. Azines, Oxazines, and Thiazines.
I. Hydroxy-Ketone dyestuffs.
J. Sulphide dyes.
K. Vat dyestuffs: Indigo and Indanthrenes.

The grouping is based on chemical relationships rather than on any similarities in dyeing properties.

A. Nitroso- and Nitro-dyestuffs

A good mordant dye is produced by the introduction of one or more hydroxyl groups into the molecule of an aromatic nitroso derivative, the chromophore being the nitroso group. Examples are: **Resorcine green,** 2:3:6-trihydroxynitrosobenzene; the three **gambines,** R = 1-hydroxy-2-nitroso-, γ = 1-nitroso-2-hydroxy-, and B = 1-nitroso-2:7-dihydroxynaphthalene. They are generally used with an iron mordant.

Examples of nitro-dyestuffs are: Picric acid (p. 443), salts of 2:4-dinitro-1-naphthol or *Martius* yellow, and the commoner naphthol yellow S or sodium 2:4-dinitro-1-naphthol-7-sulphonate (p. 534).

B. Azo-dyes

The formation of simple acidic and basic azo-dyes derived from benzene, *e.g.* the chrysoidines and tropæolines, by the coupling of a diazonium salt with a phenol or an arylamine * has been referred to in an earlier chapter (XXII, E). It is probable that the first stage in the coupling is the addition of the diazonium salt to the N atom of the amine or the O atom of the phenol or phenolic ether, *e.g.* $C_6H_5{\cdot}NEt_2$

* **Coupling does not occur between a diazonium salt and an aromatic hydrocarbon, or a halogen derivative, but the introduction of CH_3, NO_2, Cl and other groups into a phenol or amine facilitates coupling, and the presence of negative groups tends, as a rule, to make the diazonium salts more stable.**

$\rightarrow C_6H_5 \cdot NEt_2 \langle^{Cl}_{N:NC_6H_5}$, and the subsequent wandering of the N_2Ph group into the nucleus, and the elimination of hydrogen chloride (B. 1914, **47**, 1275; 1915, **48**, 1398).

The coupling of the diazonium salt with an alkaline solution of a phenol takes place more readily than with an acid solution of an amine. In the former case, however, a large excess of caustic soda has to be avoided, as this tends to transform the diazonium salt into an isodiazo oxide (p. 418), which does not couple with the phenol. The usual practice is to add sufficient caustic soda solution to the phenol to transform it into its alkali salt, and then to use sodium carbonate for neutralizing the hydrochloric acid formed during the coupling. When coupling with an amine dissolved in hydrochloric acid, sodium acetate is sometimes added during the reaction in order to react with the mineral acid and liberate the feebler acetic acid.

As already stated, the azo-group enters the para position relative to the hydroxyl, amino, or substituted amino group; if, however, the para position is already occupied, the entrant group takes up the ortho position. If neither ortho nor para position is free, coupling does not occur, unless the azo group is capable of displacing the para substituent. With di-hydroxy or di-amino derivatives of benzene coupling takes place readily when the two groups are in meta position, thus resorcinol, *m*-phenylenediamine, and *m*-toluylenediamine readily couple with diazonium salts. In the case of resorcinol the azo-groups can be introduced in stages; the first N_2Ph group takes up position 4, the second position 6, and the third position 2.

As the number of azo groups is increased the shade of the dyestuff is deepened, and at the same time coupling becomes more difficult.

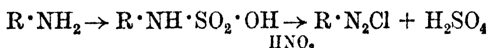
The azo dyes derived from naphthalene are of greater commercial value than those obtained from benzene. In the case of α-naphthalene derivatives the azo group takes up para (4) position, but if this is not free an ortho (2) azo compound is formed. If position 4 is free, but substituents, especially sulphonic acid groups, are present in positions 3 and 5 then the azo group enters position 2. With a β-naphthalene derivative, *e.g.* β-naphthol or β-naphthylamine, the azo-group enters position 1. Coupling with 1:2 or 2:1-amino-naphthols cannot take place.

As a rule azo-dyes are formed in solution, and are salted

out, filtered, dried, and ground. Insoluble dyes are frequently prepared on the fabric; an example of such is **para-red**, $NO_2 \cdot C_6H_4 \cdot N_2 \cdot C_{10}H_6 \cdot OH$, obtained by steeping cotton in sodium β-naphthoxide solution, squeezing out, drying, and final treatment with a 1-per-cent solution of *p*-nitrobenzenediazonium chloride. Numerous dyes of the same type are obtained by replacing the *p*-nitrobenzenediazonium chloride by the diazonium salts derived from *m*- or *o*-nitraniline, α-naphthylamine, benzidine, dianisidine, *o*-anisidine, &c. To facilitate the production of such dyes on the fabric diazotized *p*-nitraniline is sent out in the solid, stabilized form under the name of **nitrosamine red** and various other names.

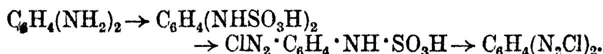
Many other sparingly soluble diazonium salts are now sent out in the solid stabilized form, *e.g.* in the form of double salts with zinc chloride with the addition of partially dehydrated aluminium sulphate to keep dry. As a rule the more soluble sulphonated diazonium salts cannot be sent out in this form. The addition of naphthalene-di- and trisulphonic acids also produces stability.

Insoluble or sparingly soluble amines can be converted into readily soluble sulphamic acids by reaction with chlorosulphonic acid and pyridine, and the products can be diazotized with elimination of the N-sulphonic group



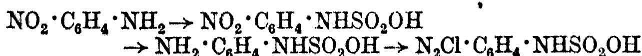
$$R \cdot NH_2 \rightarrow R \cdot NH \cdot SO_2 \cdot OH \underset{HNO_2}{\rightarrow} R \cdot N_2Cl + H_2SO_4$$

with a diamine the disulphamic acids can be diazotized in two distinct stages giving first a diazoaryl-sulphamic acid and finally a tetrazonium salt.



$$C_6H_4(NH_2)_2 \rightarrow C_6H_4(NHSO_3H)_2 \rightarrow ClN_2 \cdot C_6H_4 \cdot NH \cdot SO_3H \rightarrow C_6H_4(N_2Cl)_2.$$

The diazoaryl-sulphamic acids readily couple with β-naphthol yielding soluble dyes. With a nitroamine it is possible to obtain a diazonium salt with the diazo group in place of the nitro group by the following series of reactions, the NH_2 being converted into the sulphamic acid, the nitro group then



$$NO_2 \cdot C_6H_4 \cdot NH_2 \rightarrow NO_2 \cdot C_6H_4 \cdot NHSO_2OH \rightarrow NH_2 \cdot C_6H_4 \cdot NHSO_2OH \rightarrow N_2Cl \cdot C_6H_4 \cdot NHSO_2OH$$

carefully reduced and the product treated with one equivalent of nitrous acid.

When a diazonium salt is readily hydrolysed and cannot therefore be prepared in aqueous solution it is possible to diazotize with nitro-sulphonic acid (chamber crystals or nitrosyl sulphate) in concentrated sulphuric acid. In this way picramide, *s*-tri-nitraniline, can be diazotized. Amines in benzene solution can be diazotized by means of nitrogen peroxide, and it is claimed that this reaction is in harmony with the formula $O{:}N{\cdot}O{\cdot}NO_2$ for the peroxide (J. A. C. S. 1925, 3011.)

The following are some simple monoazo dyes derived from naphthalene. The first name is that of the amine, which is diazotized, and the second is that of the phenol, with which it is coupled:

Sudan I	= Aniline ⟶ β-naphthol.
Sudan II	= Xylidine ⟶ β-naphthol.
Crystal Ponceau B	= Naphthylamine ⟶ β-naptholdisulphonic acid G.
Ponceau 2 G	= Aniline ⟶ β-naphtholdisulphonic acid R.
Ponceau 4 GB	= Aniline ⟶ β-naphtholdisulphonic acid Sch.
Orange G	= Aniline ⟶ β-naptholdisulphonic acid G.
Orange G.T.	= Toluidine ⟶ β-naphtholsulphonic acid S.
Cochineal Scarlet	= Toluidine ⟶ α-naphtholsulphonic acid C.
Wool Scarlet R	= Xylidine ⟶ α-naphtholdisulphonic acid Sch.
Fast Red A	= Naphthionic acid ⟶ β-naphthol.
Fast Red B	= α-Naphthylamine ⟶ β-naphtholdisulphonic acid R.
Fast Red D	= Naphthionic acid ⟶ β-naphtholdisulphonic acid R.
Crumpsall Yellow	= β-naphthylaminedisulphonic acid G ⟶ salicylic acid.
Tannin Orange R	= *p*-Aminobenzyldimethylamine ⟶ β-naphthol.
Azophosphine GO	= *m*-Aminophenyltrimethylamine ⟶ resorcinol.
Alizarin Yellow	= *m*-Nitraniline ⟶ salicylic acid.
Azochromine	= *p*-Aminophenol ⟶ pyrogallol.

Very fast dyes are produced by coupling diazonium salts with **chromatropic acid,** 1:8-dihydroxynaphthalene-3:6-disulphonic acid, but they are expensive to manufacture.

Many of the monoazo dyes can be used for wool, silk, and leather direct, but can only dye cotton after mordanting. The common mordant for a basic dye is tannic acid. The phenolic dyes are used in much the same manner as alizarin (p. 541), provided two hydroxyl or one hydroxyl and one carboxyl group are present in adjacent or peri positions, and hence salicylic acid, pyrogallol, and 1:8-dihydroxy sulphonic acid are often used as the second component in the process of coupling.

Disazo Dyestuffs

Group 1. These are formed by the introduction of two azo-groups—either similar or different—into the molecule of a phenol * or amine, and are produced in two successive stages. When one of the couplings takes place in acid solution and involves the introduction of the azo-group into the ring containing the amino group, and the other takes place in alkaline solution and involves the introduction of the azo group into the ring containing hydroxyl groups, then the two couplings are always effected in the order given, as the former proceeds less readily than the latter, and is retarded to a greater extent as the components become more complex.

A good example is **Wool Black,** 6B, obtained by the successive action of diazotized sulphanilic acid in acid solution, and of diazotized α-naphthylamine in alkaline solution on 1:8-aminonaphthol-4-sulphonic acid. Other examples are:—

Resorcin Brown	= *m*-Xylidine ⟶ resorcinol ⟵ sulphanilic acid.
Naphthol Blue-black	= *p*-Nitraniline ⟶ aminonaphtholdisulphonic acid H ⟵ aniline.
Fast Brown G	= Sulphanilic acid ⟶ α-naphthol ⟵ sulphanilic acid.
Palatine Black	= Sulphanilic acid (acid solution) ⟶ 1-amino-8-naphtholdisulphonic acid H ⟵ α-naphthylamine.

The amine mentioned first is diazotized, then coupled with the middle compound, and finally the last-mentioned substance is diazotized and coupled with the monoazo dye formed from the first two.

Group 2. The members of this group are synthesised by first preparing an amino-azo compound, diazotizing the amino group in this, and coupling the product with an amine or phenol.

A complex member is **naphthol black,** $(SO_3Na)_2C_{10}H_5\cdot N:N\cdot C_{10}H_6\cdot N:N\cdot C_{10}H_4(OH)(SO_3Na)_2$, and is formed by diazotizing β-naphthylamine-6:8-disulphonic acid, coupling with α-naphthylamine, then diazotizing the resulting amino-azo compound and coupling with an alkaline solution of β-naphthol-3:6-disulphonic acid. Other examples are:—

* For influence of various groups in the phenol molecule on coupling compare *Auwers* and *Michaelis*, B. 1914, 47, 1275.

Sudan III	= Aminoazobenzene ⟶ β-naphthol.
Brilliant Crocein	= Aminoazobenzene ⟶ β-naphtholdisulphonic acid G.
Ponceau 5 R	= Aminoazobenzene ⟶ β-naphtholtrisulphonic acid.
Cloth Scarlet G	= Aminoazobenzene sulphonic acid ⟶ β-naphthol.
Fast Ponceau 2 B	= Aminoazobenzenedisulphonic acid ⟶ β-naphthol-disulphonic acid R.
Diamond Green	= Aminosalicylic acid-azo-α-naphthylamine ⟶ dihydroxynaphthalenesulphonic acid S.

As great difficulty is experienced in diazotizing naphthalene derivatives in which the amino and azo groups are ortho to one another, it is necessary to use *p*-aminoazo compounds, and hence derivatives of α-naphthylamine are commonly used.

Group 3. This group comprises the disazo dyestuffs obtained by diazotizing a primary diamine and coupling the tetrazonium salt with two molecules of an amine or phenol. The compounds of commercial importance are those derived from benzidine (*pp'*-diaminodiphenyl, Chap. XXVII) and its homologues, the tolidines. When two molecules of the same amine or phenol are used, the products are *simple* benzidine dyestuffs, *e.g.* **Congo-red** from tetrazobenzidine chloride and sodium naphthionate, $SO_3Na \cdot C_{10}H_5(NH_2)N_2 \cdot C_6H_4 \cdot C_6H_4 \cdot N_2 \cdot C_{10}H_5(NH_2)SO_3Na$.

Intermediate compounds of the type $ClN_2 \cdot C_6H_4 \cdot C_6H_4 \cdot N_2 \cdot C_{10}H_5(NH_2) \cdot SO_3Na$ can be prepared as crystalline salts, but are of no technical importance. The coupling with the second molecule of amine proceeds slowly, and may, in certain cases, take several days for completion.

The dyes derived from benzidine and certain substituted benzidines are of great commercial value, as they are **substantive dyes**; that is, they can dye cotton fabrics without the aid of a mordant. All benzidines which contain substituents in the ortho positions with respect to the amino groups can yield substantive dyes, whereas the disazo compounds derived from benzidine derivatives with meta substituents, *e.g.* *pp'*-diamino-*o*-*o'*-dicarboxylic acid or the corresponding halogen derivatives or sulphonic acids, exhibit no affinity for the vegetable fibre.

Numerous other *p*-diamines can also yield substantive dyes, *e.g.* *pp*-diaminostilbene (Chap. XXIX), $NH_2 \cdot C_6H_4 \cdot CH{:}CH \cdot C_6H_4 \cdot NH_2$; *pp*-diaminodiphenylamine, $NH(C_6H_4 \cdot NH_2)_2$; *pp*-diaminodiphenylcarbamide, $CO(NH \cdot C_6H_4 \cdot NH_2)_2$; *pp*-diaminocarbazole; *pp*-diaminofluorene and *pp*-diamino-azobenzene, $NH_2 \cdot C_6H_4N_2 \cdot C_6H_4 \cdot NH_2$. *p*-Phenylenediamine and 1:4-

and 1:5-diaminonaphthalenes also yield substantive dyes, whereas *pp*-diaminodiphenylmethane (Chap. XXVIII) and *pp*-diaminodibenzyl, $NH_2 \cdot C_6H_4 \cdot CH_2 \cdot CH_2 \cdot C_6H_4 \cdot NH_2$, do not.

The number of combinations between such diamines and various phenols, amines, and their sulphonic acids is extremely large, and only a few of the resulting substantive dyes can be mentioned:

Chrysamine G	= Benzidine ⟶ salicylic acid (2 mols.).
Diamine Black RO	= Benzidine ⟶ γ-aminonaphtholsulphonic acid (2 mols.).
Chrysophenine G	= Diaminostilbenedisulphonic acid ⟶ phenetol (2 mols.).
Cotton Yellow G	= Diaminodiphenylurea ⟶ salicylic acid (2 mols.).
Diamine brown M or **Crumpsail direct fast brown B**	= Benzidine ⟶ salicylic acid. ⟶ γ-aminonaphtholsulphonic acid (alkaline solution).
Benzopurpurin B	= Tolidine ⟶ β-naphthylaminesulphonic acid Br. (2 mols.).
Diamine blue BX or **Niagara blue BX**	= Tolidine ⟶ α-naphtholsulphonic acid NW. ⟶ aminonaphtholdisulphonic acid H.
Chicago blue 6 B or **Dianol brilliant blue**	= Dianisidine ⟶ 1:8-aminonaphthol-2:4-disulphonic acid (2 mols.).
Acid anthracene red 3 B	= *o*-Tolidinedisulphonic acid ⟶ β-naphthol (2 mols.).
Carbazol yellow	= Diaminocarbazol ⟶ salicylic acid (2 mols.).
Naphthylene red	= 1:5-Diaminonaphthalene ⟶ naphthionic acid (2 mols.).

Bismarck brown, $C_6H_4[N_2 \cdot C_6H_3(NH_2)_2]_2$ (Chap. XXII E) is a bisazo dye derived from a metadiamine, and can only be used on cotton in the presence of a tannin mordant, but dyes wool a red-brown shade.

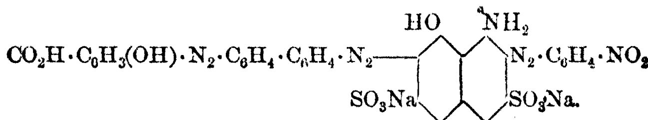
TRISAZO DYESTUFFS

These contain three azo groups. One method of preparing such compounds is by starting with a bisazo dyestuff, *e.g.* a benzidine dye, containing an amino group, diazotizing this and coupling the product with an amine or a phenol. Thus the dye produced by coupling diazotized benzidine with salicylic acid and with α-naphthylamine can be further diazotized and the product coupled with 1-naphthol-4-sulphonic acid, when the dye **benzo grey S extra** is obtained. **Columbia**

black R is obtained from tolidine with *m*-toluylenediamine and aminonaphtholdisulphonic acid γ, diazotizing the product and coupling with *m*-toluylenediamine.

A second method is to couple a diazonium salt with one of the components present in a benzidine dye; thus **Congo-brown G** is formed by allowing diazotized sulphanilic acid to couple with the resorcinol residue in the bisazo dye derived from benzidine, salicylic acid, and resorcinol.

Diamine green G or **Dianol green G**, the first green substantive dyestuff, is manufactured by coupling diazotized *p*-nitraniline with 8-hydroxy-1-naphthylamine-3:6-disulphonic acid (H acid), then coupling benzidine tetrazonium salt with this and finally with salicylic acid. Its structural formula is



TETRAKISAZO DYESTUFFS

These can be prepared by the action of two molecules of a diazonium salt on a suitable bisazo dyestuff; thus the dye derived from benzidine and resorcinol (2 mols.) couples with diazotized salicylic acid, yielding **Hessian brown BB.**

Another method of formation is the coupling of two molecules of the intermediate tetrazo compound, formed in the production of a benzidine dye, with one molecule of dihydroxydiphenyl-methane or with a similar compound.

Most of the dyestuffs are brown, and have only a limited importance.

In the benzidine dyes, as in many other series of azo dyes, the presence of chlorine atoms renders the products much faster to light. *m*-*m*-Dichlorobenzidine gives rise to the products known as **dianol reds**, and **chlorazol blues** are obtained by coupling the tetrazo derivative of dianisidine with chlorinated naphtholsulphonic acids.

Many of the direct cotton dyes are also used on wool. On cotton some exhibit sensitiveness to washing and acids, but can be rendered much faster by an " after-treatment " with either a weak chrome bath, formaldehyde or sodium thiosulphate.

A few mono-azo direct cotton dyes are known; these are mostly derived from dehydrothio-*p*-toluidine,



and its homologues or from primuline-sulphonic acid by diazotizing and coupling with salicylic acid or naphtholsulphonic acid.

Some of the more complex azo-dyestuffs are actually prepared on the fabric. This may be accomplished in one of two ways:

(*a*) *Coupling on the fibre.*—In order to obtain complex dyes, the fabric which has been dyed with a substantive dye is sometimes treated with a solution of *p*-nitrobenzenediazonium chloride. For this purpose the substantive dye must contain a residue capable of coupling with a diazonium salt.

(*b*) *Developing on the fibre.*—When the fabric has been dyed with a dyestuff containing an amino group, it is subsequently treated with nitrous acid and then with a bath of β-naphthol, when a more complex dye is actually produced on the fibre. Thus to produce **Diazo black B** the fabric is dyed with the substantive dye derived from benzidine and 1-naphthylamine-5-sulphonic acid, which is then diazotized on the fabric and developed with β-naphthol for blue-black or with *p*-phenylenediamine for brown-black shades.

Such dyes are termed **ingrain** or **ice** colours.

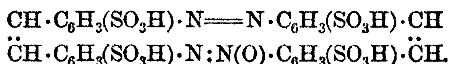
C. Stilbene, Pyrazolone, and Thiazole Dyestuffs

1. STILBENE DYESTUFFS

This group comprises a number of yellow and orange substantive dyestuffs which are relatively fast. The elucidation of the constitution is due to *A. G. Green* (J. C. S. 1904, 1424, 1432; 1906, 1602; 1907, 2076; 1908, 1721), who obtained from them diaminostilbenedisulphonic acids by reduction and benzaldehydesulphonic acids by oxidation with permanganate. By the action of hot caustic soda on *p*-nitrotoluene-*o*-sulphonic acid, **sun yellow** or **direct yellow RT** (*Walther*, 1883) is formed, and this with hypochlorite gives **Mikado yellow**, and reduced gives **Mikado orange.**

The first product formed in the condensation of *p*-nitrotoluene-*o*-sulphonic acid with alkali is a *p*-nitroso-*p*′-nitro-di-

benzyldisulphonic acid together with water. Under the influence of reducing substances present this forms *pp'*-dinitrosostilbenedisulphonic acid, which undergoes further reduction to direct yellow RT, which is an azo-azoxy derivative of stilbene,



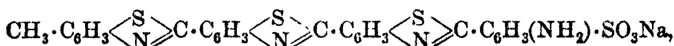
Mikado yellow is the corresponding dinitroazostilbenedisulphonic acid, which can also be formed by reducing 4:4'-dinitrostilbene-3:3'-disulphonic acid. **Stilbene orange 4 R** is the corresponding compound containing two azo groups in place of one azo and one azoxy group, and is formed when the condensation takes place in the presence of glycerol.

2. THIAZOLE DYESTUFFS

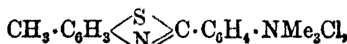
The **primulines** (*Green*, 1887) are thiazole derivatives (Chap. XXXVI 2). Primuline base itself is formed together with dehydrothiotoluidine, *p*-aminobenzothiazole,



by heating *p*-toluidine with sulphur at about 200°, and is generally used in the form of a sulphonic acid. **Primuline yellow** is probably a mixture of a di- and trithiazole derivative, *e.g.*:



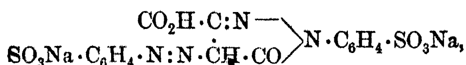
and is not fast. **Thioflavine S** is a methyl derivative of primuline, and gives canary yellow colours to tanned cotton. **Thioflavine T**, obtained from dehydrothiotoluidine, methyl alcohol, and HCl at 170° is the ammonium chloride,



and gives greenish-yellow shades.

3. PYRAZOLONE DYESTUFFS

These are mainly azo dyestuffs containing the pyrazolone ring (Chap. XXXVI 1). They are yellow dyes, fast to light but relatively expensive. **Tartrazine** (*Ziegler*, 1884),



is usually prepared by condensing ethyl oxalacetate (Chap. X F) with phenylhydrazine-*p*-sulphonic acid, coupling the product with diazotized sulphanilic acid, and hydrolysing to the free acid. Numerous other dyes can be prepared by coupling simple diazonium salts with pyrazolonesulphonic acids. **Flavazine L** is obtained from benzenediazonium chloride and 1-*p*-sulphophenyl-3-methyl-5-pyrazolone, and has the formula,



D. Di- and Triphenylmethane Dyes

The basic and acidic dyes derived from triphenylmethane have been dealt with in Chap. XXX.

The only important dyestuff of the diphenylmethane series is **Auramine O,** the ketoneimide, $NMe_2 \cdot C_6H_4 \cdot C(:NH) \cdot C_6H_4 \cdot NMe_2$, HCl, or $NMe_2 \cdot C_6H_4 \cdot C(NH_2):C_6H_4:NMe_2Cl$. This was originally prepared (*Kern* and *Caro*, 1883) by heating *Michler's* ketone, tetramethyl-4:4′-diaminobenzophenone, with ammonium and zinc chlorides at 160°, but is now generally manufactured by fusing tetramethyldiamino-diphenylmethane with sulphur, ammonium chloride, and common salt, whilst ammonia is passed through the mass; H_2S is formed, and the CH_2 group gives rise to the C:NH group. **Auramine G** is the corresponding compound derived from *o*-toluidine.

The following dyes are derivatives of diphenylnaphthylmethane, $CHPh_2 \cdot C_{10}H_7$. **Victoria blue B,** obtained by condensing phenyl-α-naphthylamine (p. 532) with tetramethyl-4:4′-diaminobenzhydrol or tetramethyl-4:4′-diaminobenzophenone chloride, is $C_6H_5 \cdot NH \cdot C_{10}H_6 \cdot C(C_6H_4 \cdot NMe_2):C_6H_4:NMe_2Cl$. **Victoria blue R** is obtained in a similar manner from ethyl-α-naphthylamine, and **night blue** from tetraethyldiaminobenzophenone chloride and *p*-tolyl-α-naphthylamine. These blues are not very fast to light, but give very bright shades. **Wool green** is formed by condensing G salt (p. 534) with tetramethyldiamino-benzophenone chloride.

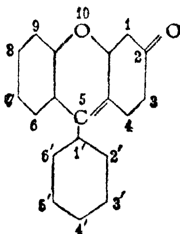
E. Xanthene Dyestuffs

These dyestuffs, which can be regarded as derivatives of diphenylmethane oxide or xanthene (Chap. XXXVIII B), contain the pyrone ring C<(C:C, C:C)>O. They are usually divided into the two groups—

1. The **pyronines,** or derivatives of diphenylmethane, and
2. The **phthaleines,** or derivatives of triphenylmethane.

The formation and structure of the phthaleines have been dealt with in Chap. XXX. The chief members of this class are the eosines, the rhodamines, and galleine.

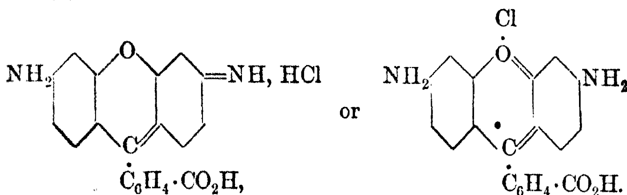
The following numbering of the atoms in the fluoresceïn skeleton is adopted:—



This numbering is not the same as that given in *Richter's* Lexicon, but is analogous to that adopted for acridine, phenazine, &c.

Uranine or sodium fluoresceïn is the sodium derivative of the 8-hydroxy-2′-carboxylic acid. **Eosin A** is 1:3:7:9 tetrabromofluoresceïn. **Spirit eosin** and **Eosin S** are the corresponding methyl and ethyl esters. **Eosin BN** is potassium 3:7-dinitro-1:9-dibromofluoresceïn. **Erythrosin G** is potassium 1:9-diiodofluoresceïn, **Erythrosin** is 1:3:7:9-tetraiodofluoresceïn. **Phloxine P** is potassium 4′:5′-dichloro-1:3:7:9-tetrabromofluoresceïn. **Rose Bengal** is the corresponding tetraiodo compound. **Phloxine** is potassium 3′:4′:5′:6′-tetrachloro-1:3:7:9-tetrabromofluoresceïn. **Galleïn or alizarin violet,** from gallic acid and phthalic anhydride, is 1:9-dihydroxyfluoresceïn. **Coeruleïn** is galleïn anhydride formed by the elimination of water from the OH of the carboxyl group and hydrogen in position 4.

The **Rhodamines** or aminophthaleïns contain NH_2 and NH or substituted NH_2 and NH groups in place of the ·OH and :O groups of fluoresceïn. The bases themselves probably have a lactone structure, but the salts (dyes) may be represented by para or ortho quinonoid formulæ; in the latter case the oxygen atom becomes tetravalent.



The numbering is the same as in the fluoresceïn skeleton. The rhodamines are manufactured by condensing phthalic anhydride with substituted aminophenols. The presence of a carboxylic group in the salts and hence a quinonoid structure is indicated by the readiness with which the dyes yield alkyl derivatives, which are readily hydrolysable, *i.e.* esters; these are also coloured. If the dyes were lactones the products formed on alkylation would be quaternary ammonium salts, which should not be readily hydrolysed.

Rhodamine B contains two NEt_2 groups in positions 2 and 8. **Rhodamine 3 B** is the corresponding ethyl ester. **Rhodamine 6 G** is the ester containing two NHEt groups in 2 and 8 positions. **Rhodamine S** is the chloride of the dimethylamino compound containing the group $\cdot CH_2 \cdot CH_2 \cdot CO_2H$ (derived from succinic acid) attached to C No. 5. **Violamines** contain phenyl and tolyl, and sulphonated phenyl groups attached to the N atoms in positions 2 and 8.

Dyes with an ester structure such as Rhodamine 3 B or 6 G or Eosin S are as a rule faster and more stable, as the conversion of the ·COONa group to ·COOEt lessens the tendency to the formation of colourless lactones. Such dyes can be used as direct dyes for cotton.

The pyronines are of but little importance, and are formed by condensing alkylated *m*-aminophenols with aliphatic aldehydes or acids, *e.g.* **pyronine G** from formaldehyde and dimethyl-*m*-aminophenol and subsequent oxidation.

F. Acridine and Quinoline Dyes

The chromogene in the acridine dyestuffs is the acridine ring (Chap. XXXVIII B) with an orthoquinonoid structure, $C_6H_4<\genfrac{}{}{0pt}{}{N=}{CH}>C_6H_4$. They are analogous to the xanthene dyestuffs, and by replacing the H of the CH group by phenyl, triphenylmethane derivatives are obtained. The only compounds of commercial importance are the amino or substituted amino derivatives, with the nitrogen atoms in the positions para to the CH group.

Acridine yellow,* 2:8-diamino-3:7-dimethylacridine hydrochloride, is a basic yellow dye obtained by condensing *m*-toluylenediamine with formaldehyde and oxidizing the resulting leuco-base. The corresponding 5-phenyl derivative is **benzoflavine. Acridine orange,** 2:8-tetramethyldiaminoacridine zinc chloride, is obtained from *m*-aminodimethylaniline and formaldehyde and **Acridine orange R** extra is the corresponding 5-phenyl derivative obtained by using benzaldehyde. **Phosphine** or leather yellow is impure chrysaniline, 2:4′-diaminophenylacridine, and is obtained as a by-product in the manufacture of fuchsine or magenta (Chap. XXX 2).

Common quinoline dyes are mentioned on p. 586.

Cyanine dyes.—The cyanine dyes are of great value as sensitizers for the photographic plate, e.g. in the production of panchromatic plates, *i.e.* plates which are nearly equally sensitive to all parts of the spectrum: pinacyanol which sensitizes right into the red and pinaverdol which sensitizes through the green into the red, are two of the oldest dyes, but numerous others have been prepared during 1917 to 1929, and the structure of many has been elucidated by *Mills* and his co-workers both by processes of oxidation and by syntheses.

They all contain two heterocyclic nitrogen-containing rings, the nitrogen in one being in the tervalent state and in the other in the quinquevalent or ammonium salt form. In some of the newer dyes a nitrogen-sulphur ring, *e.g.* benzthiazole ring may replace one or both of the rings. As a rule the two rings are quinoline rings, but a few dyes containing pyridine rings are known.

* The numbering is exactly similar to that of fluorescein derivatives, (p. 922), the N atom occupying the position of the pyrone oxygen in fluorescein.

The two rings may be directly united, but usually are joined by the ·CH: or ·CH:CH·CH: group, or a longer chain containing alternate single and double linkings. The colour of the dyes is attributed to these alternate double linkings being in conjugation with linkings in the rings. The sub-division of the dyes is as follows (cf. *Koenigs*, B. 1922, 3293; *Mills*, J. C. S. 1928, 1918):—

I. Nitrogen rings directly united = **Apocyanines.**

II. Nitrogen rings attached by a ·CH: group:

(*a*) 2:2′ attachment = **Pseudocyanines.**
(*b*) 2:4′ attachment = **Isocyanines.**
(*c*) 4:4′ attachment = **Cyanines.**

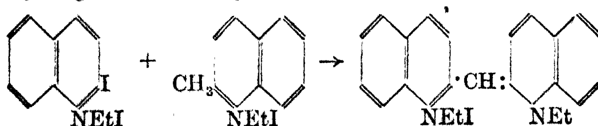
III. Nitrogen rings united by a :CH·CH:CH· group = Carbocyanine dyes.

(*a*) 2:2′ attachment = 2:2′-**carbocyanines.**
(*b*) 2:4′ attachment = **Dicyanines.**
(*c*) 4:4′ attachment = **Kryptocyanines.**

IV. **Thiocyanines.**

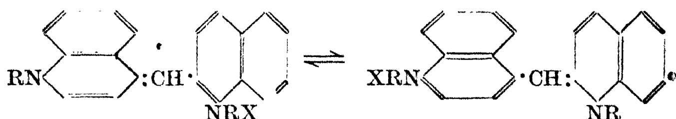
I. **Apocyanines.**—(*a*) Xanthoapocyanines with 3:2′-attachment and (*b*) Erythroapocyanines with 3:4′-attachment. A mixture of two such dyes is formed by the action of alcoholic potash on a quinoline ethiodide. The structure of the latter has been established by *Mills* and *Ordisch* (J. C. S. 1928, 81) by oxidizing it with iodine to 3:4′-diquinolyl $(C_9H_6N)_2$ which has been directly synthesised.

II. (*a*) The **pseudocyanines** can be prepared by the action of alcoholic potash on 2-iodoquinoline methiodide and quinaldine methiodide (*Hamer*, J. C. S. 1928, 206), and similar compounds. They exert a sensitizing action in the bluish-green region of the spectrum. The condensation occurs between the iodine atom in position 2 of one nucleus and a hydrogen atom of the methyl group in position 2 of the second nucleus, also elimination of HI from the ammonium iodide and hydrogen of the CH_3.



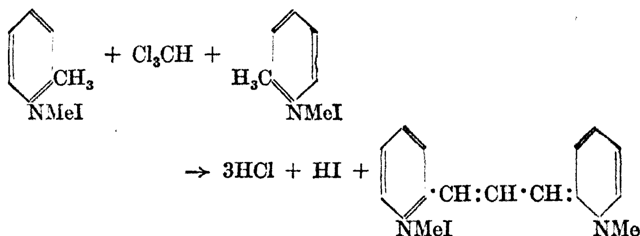
(*b*) **Isocyanines** can be synthesised by a process similar to the above but using 4-chloroquinoline alkyl iodides. The structure has been confirmed by oxidation, *e.g.* dimethylisocyanine acetate when oxidized yields 1-methyl-2-quinolone (NMe in position 1 and CO in position 2) and cinchoninic acid methochloride (NMeCl in 1 and $C{\cdot}CO_2H$ in 4), *Mills* and *Wishart*, J. C. S. 1920, 579).

Isocyanines and all cyanines which are not symmetrical are tautomeric as indicated by the following scheme:—



III. **Carbocyanines.**

(*a*) 2:2′-**Carbocyanines.**—One of the simplest of these is 2:2′-carbopyridine cyanine I obtained by the action of chloroform and potash on α-picoline alkyl iodides (B. 1929, 2724)



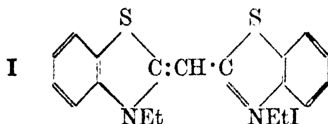
By using γ-picoline the isomeric 4:4′-cyanine is formed. In all the syntheses of carbocyanines the chain, ·CH:CH·CH:, is built up from the two reactive methyl groups present in two substituted pyridine or quinoline rings, and a third carbon atom introduced in the form of chloroform, formaldehyde, ethyl orthoformate or the complex diorthoformylmethylaminodiphenyl disulphide, $O{:}CH{\cdot}NMe{\cdot}C_6H_4{\cdot}S{\cdot}S{\cdot}C_6H_4{\cdot}NMe{\cdot}CH{:}O$, in pyridine solution (*Mills* and *Odams*, J. C. S. 1924, 1914).

One of the first known cyanine dyes, pinacyanol, is a 2:2′-carbocyanine with quinoline rings; it is formed by the action of potash and formalin on mixtures of ethiodides of quinoline and quinaldine. Its structure follows from the fact that

on oxidation it yields 1-ethyl-2-quinolone (NEt in 1 CO in 2) and quinaldinic acid ethyl nitrate ($NEtNO_3$ in 1 and $C{\cdot}CO_2H$ in 2), *Mills* and *Harmer*, J. C. S. 1920, 1550), and hence is a 2:2′-carbocyanine with two quinoline residues and NEt in position 1 and NEtX in position 1′. It has been synthesised from quinaldine ethiodide and ethyl orthoformate in presence of acetic anhydride and zinc chloride.

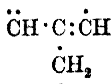
Krypocyanines can be synthesised in a similar manner, using 4-methylquinoline (lepidine) alkyl iodides (*Mills* and *Braunholz* (J. C. S. 1923, 2804), and dicyanines by using a mixture of alkyl nitrates of quinaldine and lepidine, in this synthesis small amounts of 2:2′ and 4:4′-carbocyanines are formed, but the chief product is the 2:4′- or dicyanine (*Mills* and *Odams*, J. C. S. 1924, 1913).

IV. **Thiocyanines**, *e.g.* diethylthiocyanine, I, can be synthesised by the action of ethyl malonate on *o*-aminothiophenol, converting the product into the mono ethiodide, removing HI by alkali, and then converting the second N into its ethiodide (*Mills*, 1922, 455, 1489).



Thiocarbocyanines (*König*, B. 1928, 2065; *Hamer*, J. C. S. 1928, 3160) and selenocarbocyanines (J. C. S. 1928, 2313) have been formed and also cyanines from methylnaphthethiazoles. Also compounds containing the chain :CH·N:N· in place of :CH·CH·CH· (*Fuchs* and *Granang*, B. 1928, 57). Some of these latter are desensitizers towards the photographic plate.

Neocyanines contain three quinoline rings attached in position 4, 4′, and 4″ to the chain:



(*Hamer*, J. C. S. 1928, 1472). They are obtained by the action of ethyl orthoformate on lepidine alkyl salts.

G. Indamine and Indophenol Dyestuffs

The indophenol and indamine dyestuffs are derivatives of phenylated *p*-quinone mono- and di-imides respectively, $O:C_6H_4:NPh$ and $NH:C_6H_4:NPh$ (Chap. XXV F.)

Indamines: Phenylene blue, $NH_2\cdot C_6H_4\cdot N:C_6H_4:NH_2Cl$, obtained by oxidizing a mixture of aniline and *p*-phenylenediamine, when the hydrogen para to the amino group in aniline, and three of the four hydrogen atoms of the amino groups of the diamine are removed by oxidation, and union of the two amine residues takes place. **Bindschedler's green** is the corresponding tetramethyl derivative. **Toluylene blue,** $NMe_2\cdot C_6H_4\cdot N:C_6H_2Me(NH_2):NH_2Cl$, obtained by oxidizing dimethyl-*p*-phenylenediamine and *m*-toluylenediamine is of interest on account of its relationship to the eurhoidine, neutral red (p. 930). Indamines are also formed by oxidizing a mixture of an arylamine (or *m*-diamine) with *p*-nitrosodimethylaniline instead of the *p*-diamine.

The **Indophenols** can be formed in a similar manner by oxidizing a mixture of a phenol (or naphthol) with a paradiamine or with *p*-nitrosodimethylaniline. The only dye of technical importance is **indophenol blue,** $NMe_2\cdot C_6H_4\cdot N:C_{10}H_6\cdot O$, obtained by condensing α-naphthol with *p*-nitrosodimethylaniline. It is sometimes used in combination with indigo, as the process of dyeing is exactly analogous. It is a typical vat dye.

H. Azine, Oxazine, and Thiazine Dyestuffs

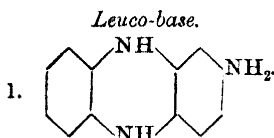
Practically all these dyestuffs are basic dyes, and are used in the form of salts. They are readily reduced to leuco-compounds, which re-oxidize in the presence of air. These leuco-compounds are amino or substituted amino derivatives of dihydrophenazine, phenoxazine, and phenthiazine respectively (Chap. XXXIX).

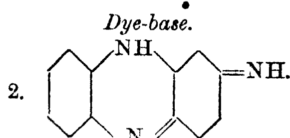


In all cases the amino or substituted amino groups occupy position 2.*

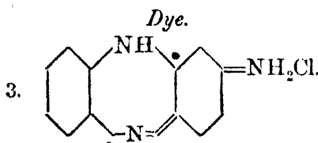
* For purposes of orientating the numbering of the atoms is exactly similar to that in the case of fluoresceïn (p. 922) and acridine dyes, the CH in these being replaced by N.

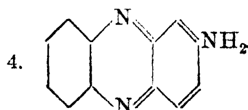
The relationships of the leuco-base (1), dye-base (2), and dyestuff (3) are rendered clear by a glance at the formulæ for the azine compounds:



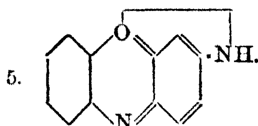


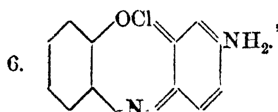
An orthoquinonoid structure for the dye-base and dye is also possible, viz. (4). The oxazine and thiazine dyes can be





represented by formulæ analogous to 3, but with O and S in place of the NH group of the middle ring. If orthoquinonoid formulæ are used for the dye-bases, union between O or S and the substituting NH group in position 2 must be assumed, *e.g.* (5), but not for the salts, *e.g.* (6). The orthoquinonoid





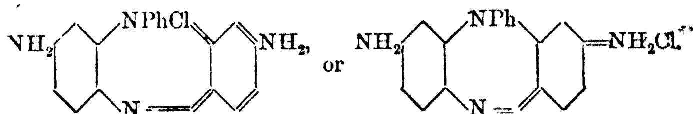
formulæ for the salts are now generally adopted; that for the azine salt represents the upper nitrogen in the middle ring, formula 4, as combining with the acid, *e.g.* HCl, and becoming quinquevalent. Such salts, containing quinquevalent N and tetravalent O or S, are usually termed phenazonium, oxazonium, and thiazonium salts.

1. AZINE DYESTUFFS

1. The azine dyestuffs comprise the following sub-groups:—

(*a*) The **Eurhoidines.**—Most of these are diamino or substituted diamino derivatives, but have no alkyl or aryl group attached to the nitrogen atom in position 10.

(*b*) The **Safranines** are all 2:8-diamino derivatives, and in addition have a phenyl or substituted phenyl group attached to the nitrogen in position 10. They are phenyl-diamino-phenazonium salts, often with substituents in the benzene rings or in the amino groups. The formula of the simplest safranine is therefore



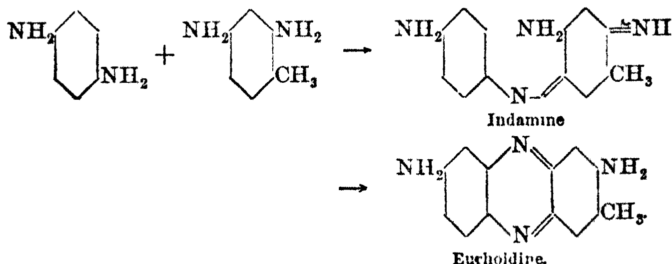
Safranines may also be derived from azines in which one or both of the benzene rings are replaced by naphthalene residues.

(*c*) The **Aposafranines** also have an alphyl or aryl group attached to nitrogen in position 10. They are, however, mono-amino derivatives, and always contain one naphthalene residue.

(*d*) The **Indulines** contain 3 or 4 amino groups.

(*a*) THE EURHOIDINES

These form a small and unimportant class. The dye-bases are only weak bases, and form red mono-acid salts. They are usually prepared by the oxidation of indamines. One of the best known is **toluylene red.** By the oxidation of a mixture of *p*-phenylenediamine and *m*-toluylenediamine an indamine (p. 928) is formed:



Neutral red. $NMe_2{\cdot}C_6H_3\langle{N(HCl) \atop N}\rangle C_6H_2Me{\cdot}NH_2$, is ob-

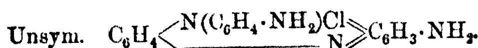
tained by the further oxidation of toluylene blue (p. 928) and neutral violet, $NMe_2 \cdot C_6H_3 \langle {N(HCl) \atop N} \rangle C_6H_3 \cdot NH_2$, from *p*-aminodimethylaniline and *m*-phenylenediamine. The constitution of toluylene red follows from the fact that when diazotized and warmed with alcohol it yields a methylphenazine identical with that obtained by oxidizing the methyldihydrophenazine synthesised from catechol (1:2-dihydroxybenzene) and *m*-toluylenediamine ($Me:NH_2:NH_2 = 1:3:4$).

(*b*) SAFRANINES

Considerable discussion has taken place with reference to two important points connected with the structure of the safranines, viz: (1) the ortho- or paraquinonoid structure of the dyes, and (2) the symmetrical or unsymmetrical positions of the amino groups.

Nietski's statement of the existence of two isomeric monomethyl safranines was used as an argument in favour of the unsymmetrical arrangement of the two amino groups, but *Körner* and *Schmidt's* proof of the identity of the two compounds lent support to the symmetrical structure which has been since confirmed by *Hewitt*.


Sym. $NH_2 \cdot C_6H_3 \langle {NPhCl \atop N} \rangle C_6H_3 \cdot NH_2$.


Unsym. $C_6H_4 \langle {N(C_6H_4 \cdot NH_2)Cl \atop N} \rangle C_6H_3 \cdot NH_2$.

By the ordinary methods of diazotizing only one NH_2 group is removed from safranine, and for some time this was regarded as an argument in favour of the paraquinonoid formula which contains only one true $\cdot NH_2$ group. Subsequent experiments have proved that a second amino group can be removed by diazotizing in the presence of concentrated sulphuric acid, and this has given support to the orthoquinonoid formula which contains two free amino groups. The readiness with which the leuco-bases are oxidized to the dye-bases is also in harmony with the ortho structure.

When safranine sulphate is treated with barium hydroxide the green base, safranine hydroxide is formed, and when this is heated water is eliminated, and a base practically free from

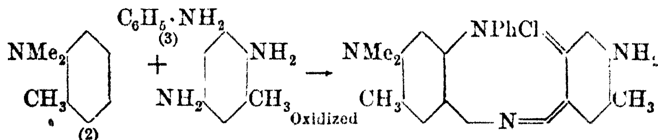
oxygen is obtained. This has been urged as an argument in favour of the para constitution, as it involves the elimination of water from $:NH_2OH$ and the formation of $:NH$. With an orthoquinonoid constitution the formation of the anhydro base involves either a molecular rearrangement into the para-quinonoid form followed by loss of water or the elimination of water directly and union between the nitrogen atoms in positions 2 and 5.

The safranines can be prepared by a variety of methods:

1. They are formed by oxidizing indamines in the presence of primary arylamines.

2. By oxidizing 4:4′-diaminodiphenylamine in the presence of primary arylamines.

3. By oxidizing a mixture of a *p*-diamine (1 mol.) with a monamine (2 mols.) This last is the ordinary commercial method, and it is essential that one of the amino groups in the diamine shall be unsubstituted, and that one of the monamines (2) taking part shall have the position para to the NH_2 group free. The second monamine (3) may have a para substituent, but the amino group itself must be unsubstituted, *e.g.*:



Safranine T, 3:7-dimethyl-2:8-diamino-10-phenylphenazonium chloride, is made by oxidizing a mixture of equimolecular proportions of *o*-toluidine and *p*-toluylene-diamine to an indamine and subsequent oxidation of this to the safranine. It is also frequently made from the oil which distils over during the manufacture of magenta. It can be diazotized and coupled with β-naphthol when the important substantive dye known as **indoine blue** is formed.

Safranine MN is 3-methyl-2-amino-8-dimethylamino-10-phenylphenazonium chloride; **Amethyst violet** contains NEt_2 groups in positions 2 and 8, and is formed by oxidizing a mixture of diethyl-*p*-phenylenediamine, diethaniline, and aniline; **Mauveine** is of historical interest as the first aniline dye to be prepared (*Perkin*, 1856), it is the safranine dye, 3-methyl-2-amino-8-anilino-10-tolylphenazonium chloride.

4. Another general method of preparing safranines is by the oxidation of a mixture of a *p*-nitrosodialkylaniline with secondary bases derived from *m*-phenylenediamine, thus nitrosodimethylaniline (3 mols.) and diphenyl-*m*-phenylenediamine (2 mols.) yield *p*-aminodimethylaniline (1 mol.) and **indazine M** (2 mols.), $NMe_2 \cdot C_6H_3 \langle {NPhCl \atop N} \rangle C_6H_3 \cdot NHPh$. The following dyes are manufactured by this process:—

Fast neutral violet B, 2-dimethylamino-8-ethylamino-10-ethylphenazonium chloride, from *p*-nitrosodimethylaniline and diethyl-*m*-phenylenediamine; **Metaphenylene blue,** 2-dimethylamino-8-tolylamino-10-tolylphenazonium chloride, from the same nitroso compound and di-*o*-tolyl-*m*-phenylenediamine; **Naphthazine blue,** 2-methylamino-8-naphthylamino-10-naphthylphenazonium chloride; **Basle blue R,** 2-dimethylamino-8-tolylamino-10-tolylnaphthazonium chloride, is obtained from the nitroso compound and 2:7-ditolylnaphthylenediamine, $C_{10}H_6(NH \cdot C_7H_7)_2$, and yields the sulphonated dye, **Basle blue S.**

5. Safranines can also be formed by fusing aminoazo compounds with primary arylamines and their salts.

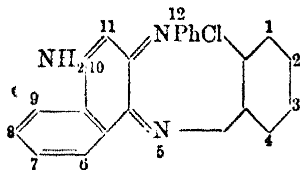
Naphthyl blue or **Milling blue,** a diphenylated dinaphthosafranine, $NHPh \cdot C_{10}H_5 \langle {NPhCl \atop N} \rangle C_{10}H_5 \cdot NHPh$, is formed from benzeneazo-α-naphthylamine, α-naphthylamine and aniline hydrochloride, and is used in the form of a sulphonic acid. **Magdala red** is a diamino-naphthyl-dinaphthazonium chloride, $NH_2 \cdot C_{10}H_5 \langle {N(C_{10}H_7)Cl \atop N} \rangle C_{10}H_5 \cdot NH_2$, and is used to a certain extent on silk.

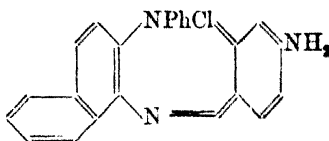
The safranines are beautiful crystalline compounds with a metallic green lustre, are readily soluble in water, and dye yellowish-red, violet, and blue, and for cotton usually require a tannin mordant.

(c) APOSAFRANINES. (Cf. p. 930)

These are usually divided into the **rosindulines** and **isorosindulines.** In the former the amino group is attached to a naphthalene residue, and in the latter to a benzene nucleus. The two groups give respectively red and blue shades.

Many contain alphyl or aryl substituents in the amino group.

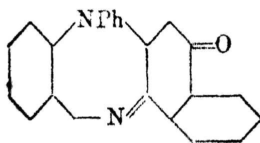




as orthoquinonoid salts.

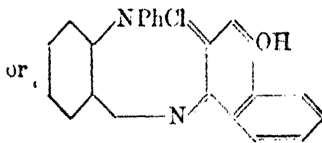
The aposafranines are formed by methods exactly analogous to numbers 4 and 5, given under safranines.

Azocarmine G, formed by fusing benzeneazo-α-naphthylamine with aniline and its hydrochloride and subsequently sulphonating, is sodium phenylrosindulinedisulphonate. **Azocarmine B** is the sodium salt of the corresponding trisulphonic acid. **Rosinduline 2 G,** obtained by heating the acid from Azocarmine B with water at 160–180°, is the sodium salt of a monosulphonic acid of rosindone, which is the oxygen analogue of rosinduline, *e.g.*:



Paraquinonoid base

or



Orthoquinonoid salt

Rosinduline G is an isomeric monosulphonate, and both compounds are important wool dyes. **Induline scarlet,** prepared by melting the azo derivative of monoethyl-*p*-toluidine with α-naphthylamine hydrochloride, has ethyl in place of phenyl attached to N in position 12, and methyl in position 3. It is frequently used in conjunction with formaldehyde hydrosulphite and rongalite for discharging colours.

Neutral blue, a typical isorosinduline, contains the NMe_2 in position 2, and is obtained by heating nitrosodimethylaniline with phenyl-β-naphthylamine.

(d) INDULINES

The first induline was prepared in 1863 by *Dale* and *Caro* by heating aniline hydrochloride with sodium nitrite, and was subsequently (*Martius* and *Griess*, 1866; *Hoffmann* and *Geyger*, 1877) shown to be formed by the action of aniline hydrochloride on aminoazobenzene at 160°. The group comprises blue, violet, and black dyestuffs, which are usually prepared by heating an aminoazo compound with a primary arylamine and its salt, usually under pressure. When a *p*-phenylenediamine is used basic indulines are formed. All the products are insoluble in water, but on sulphonation give water soluble acid dyes.

The formation of aposafranines, safranines, and indulines from aminoazo compounds and monoamine salts probably proceeds in several stages. In the case of aminoazobenzene itself:

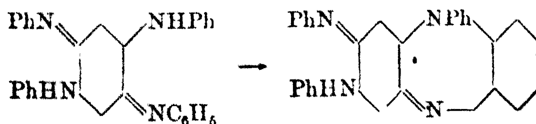
1. The isomerization of the *p*-azo compound to the hydrazone form (cf. p. 431) $NH_2{\cdot}C_6H_4{\cdot}N{:}N{\cdot}C_6H_5 \rightarrow NH{:}C_6H_4{:}N{\cdot}NHC_6H_5$.

2. Molecular rearrangement during which the $\cdot NHC_6H_5$ group exchanges place with an ortho H atom of the nucleus (cf. p. 423), $NH{:}C_6H_4{:}N{\cdot}NHC_6H_5 \rightarrow NH{:}C_6H_3(NHC_6H_5){:}NH$, whereby an anilo derivative of *p*-quinone is formed.

3. The elimination of ammonia from the primary amine and the NH groups, and the formation of quinone anilides, $C_6H_5N{:}C_6H_3(NHC_6H_5){:}NC_6H_5$, 2-anilinoquinone-1:4-dianilide.

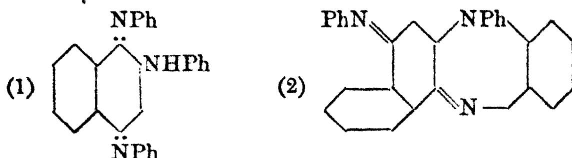
4. The formation of a dianilino derivative, *e.g.* 2:5-dianilinoquinone-1:4-dianilide, $C_6H_5N{:}C_6H_2(NHC_6H_5)_2{:}NC_6H_5$, by the removal of hydrogen from the quinone nucleus and aniline. This probably occurs at the expense of the aminoazo compound, which becomes reduced to *p*-phenylenediamine.

5. The final condensation of the dianilinoquinone anilide,

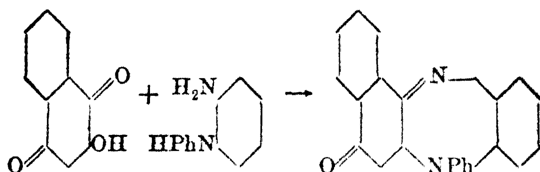


and on further heating more anilino groups are introduced,

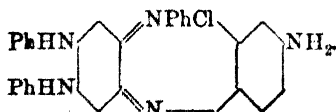
and various indulines are formed. When benzeneazo-α-naphthylamine and aniline hydrochloride are used the anilino dianilide (1) is formed, which condenses to (2):



If benzeazo-α-naphthylamine is heated with aniline and alcohol under pressure, rosinduline (p. 934) itself is formed, and this with hydrochloric acid under pressure yields rosindone (p. 934), which can be synthesised from hydroxy-α-naphthaquinone and phenyl-o-phenylenediamine:



Fast blues R or **B** are made from aminoazobenzene, aniline, and aniline hydrochloride by heating for different periods; the longer the heating the bluer the shade. They are insoluble and are largely used as pigments. The **soluble fast blues** obtained on sulphonation are important dyes for wool, silk, and can also be used for tannin cotton. The **printing blues, acetin blues,** and **laevuline blues** are solutions of the fast blues in ethyl tartaric acid, acetin, and laevulic acid respectively, and are used for cotton printing. **Indamine blue** is a basic dye obtained by using *p*-phenylenediamine instead of aniline, and has the structure:



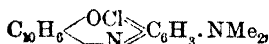
The **nigrosines** are made by heating nitrobenzene or nitroso-

phenol, aniline, and aniline hydrochlorides with iron filings, and are used for pigments and shoe polishes.

Aniline black is probably an azine dye (for structure see *Green, J. S. Dyers*, 1913, 105, 338), and is produced by oxidation of aniline on the fabric.

2. OXAZINE DYESTUFFS. (Cf. p. 928)

The first oxazine dyestuff to be manufactured was **Meldola's blue, New blue R, Cotton blue R.**

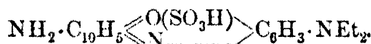


and is obtained by condensing β-naphthol (1 mol.) with an alcoholic solution of p-nitrosodimethylaniline.

Capri blue GN, obtained from nitrosodimethylaniline and dimethyl-m-amino-resorcinol, is

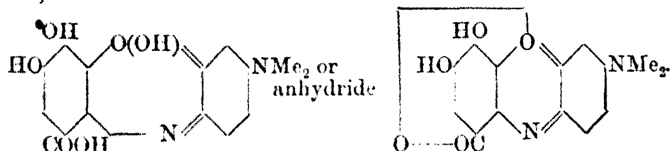


Nile blue A, from nitrosodiethyl-m-aminophenol and α-naphthylamine,



Nile blue B, obtained by using benzyl-α-naphthylamine, contains NHBz in place of NH_2.

Gallocyanine DH, from nitrosodimethylaniline and gallic acid,

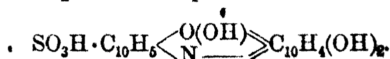


Delphin blue, obtained from gallocyanin by the action of aniline and subsequent sulphonation, contains $NH \cdot C_6H_4 \cdot SO_3NH_4$ in place of CO_2H.

Gallamine blue paste, $CO \cdot NH_2$ in place of COOH of gallamine.

Correine RR, the NEt_2 analogue of gallamine blue.

—**Alizarine green G,** from β-naphthaquinone-sulphonic acid and 1-amino-2-naphthol-6-sulphonic acid:



$$SO_3H \cdot C_{10}H_5 \lessdot \begin{matrix} O(OH) \\ N \end{matrix} \gtrdot C_{10}H_4(OH)_2.$$

Alizarin green B is an iosmeride.

All the latter compounds are mordant dyes, and can be used in the same manner as alizarin.

3. THIAZINE DYESTUFFS. (Cf. p. 928)

Lauth's violet (1876), the first member of this group to be prepared, has no commercial value. It is 2:8-diamino-thiazonium chloride, $NH_2 \cdot C_6H_3 \lessdot \begin{matrix} SCl \\ N \end{matrix} \gtrdot C_6H_3 \cdot NH_2$, and its constitution was established by *Bernthsen* (A. 1885, **230**, 73) by the following synthesis: Thiodiphenylamine and sulphur give anhydro-thiodiphenylamine. This can be nitrated to a dinitro compound, which can be reduced to the corresponding diamine identical with the leuco-base derived from *Lauth's* violet.

Methylene blue B is 2:8-tetramethyldiaminothiazonium chloride, and is manufactured by the modern process of oxidizing a mixture of dimethyl-*p*-phenylenediamine and dimethylaniline in the presence of sodium thiosulphate and zinc chloride.

It is an important dye for tannin cotton, it is used as a stain in microscopy, and as the free base finds internal use in medicine.

New methylene blue N, obtained by using monoethyl-*o*-toluidine instead of dimethylaniline, is 1:9-dimethyl-2:8-diethylaminothiazonium chloride. **Methylene green** is the 6-nitro derivative obtained by the action of nitrous acid on methylene blue B. **Thionine blue** is the trimethylethyl analogue of methylene blue. **Brilliant alizarine blue GR** is $NMe_2 \cdot C_6H_3 \lessdot \begin{matrix} S(OH) \\ N \end{matrix} \gtrdot C_{10}H_3(OH)_2 \cdot SO_3Na$, and **Indochromogene S,** $NEt_2 \cdot C_6H_3 \lessdot \begin{matrix} S(SO_3Na) \\ N \end{matrix} \gtrdot C_{10}H_3(OH)_2 \cdot SO_3Na$, is obtained by condensing *p*-aminodiethylaniline with 1:2-naphthaquinone-4:6-disulphonic acid in dilute alkaline solution.

I. Hydroxyketone Dyestuffs

The best known members of this class are the hydroxyanthraquinone or alizarine dyes (Chap. XXXII A). They are all phenolic substances, and hence acidic dyes, and contain two hydroxyls in ortho positions. On cotton they are used as mordant dyes, *i.e.* they are used for producing **lakes** with oxides of aluminium, chromium, iron, tin, &c., on the fabric. (For nature of lakes cf. *Pfeiffer*, A. 1911, **383**, 92; 1913, **398**, 137). The colour produced depends, therefore, not only on the particular dye used but also upon the mordant.

The following dyes are derived from ketones less complex than anthraquinone:—

Alizarin yellow C (gallacetophenone), 2:3:4-trihydroxyacetophenone, is obtained by heating pyrogallol with acetic acid. **Alizarin yellow A** is the corresponding trihydroxybenzophenone. **Alizarin black S** is 1:2-dihydroxy-5:8-naphthaquinone or naphthazarine (p. 535).

Alizarin derivatives.—In addition to alizarin, numerous other ortho-hydroxy derivatives of anthraquinone are used as dyestuffs, *e.g.* compounds containing 3, 4, or even 6 hydroxyl groups. When anthraquinone-β-sulphonic acid is further sulphonated, a mixture of 2:6- and 2:7-disulphonic acids is formed; the two acids can be separated by means of their sodium salts, and when fused with alkali the former yields 1:2:6-trihydroxyanthraquinone, **flavopurpurin** or alizarin X, and the latter the 1:2:7 isomeride known as **anthrapurpurin.** The 1:2:4 compound known as **purpurin** is found in madder, and can be obtained by oxidizing alizarin with sulphuric acid and MnO_2. The 1:2:3 compound, **anthracene brown** (anthragallol) is obtained by condensing benzoic and gallic acids in sulphuric acid solutions, and is usually accompanied by some 1:2:3:5:6:7-hexahydroxyanthraquinone or **anthracene brown SW.**

Alizarin bordeaux B, 1:2:6:8-tetrahydroxyanthraquinone, is obtained by oxidizing alizarin with fuming sulphuric acid, and hydrolysing the resulting sulphonic acid with 80 per cent acid, and when oxidized with sulphuric acid and MnO_2 it yields **anthracene blue WR,** 1:2:4:5:6:8-hexahydroxyanthraquinone.

Numerous sulphonic acids, obtained by heating the abovementioned dyestuffs with fuming sulphuric acid, are known.

Alizarin itself yields **alizarin red S** or **alizarin carmine,** sodium 1:2-dihydroxyanthraquinone-3-sulphonate. **Alizarin garnet** is 1:2-dihydroxy-4-amino-anthraquinone, and is obtained by nitrating alizarin dibenzoate, hydrolysing and reducing with sodium sulphide. **Alizarin SSS** is sodium 1:2:6-trihydroxyanthraquinone sulphonate.

Alizarin irisol $C_6H_4{:}C_2O_2{:}C_6H_2(OH){\cdot}NH{\cdot}C_6H_3Me{\cdot}SO_3Na$, is formed by condensing 1:4-dihydroxyanthraquinone (quinizarin) with *p*-toluidine and sulphonating the product. **Alizarin sky blue B** is the corresponding 2-bromo derivative. **Alizarin viridine** is 1:2-dihydroxy-5:8-di-*p*-toluidino-anthraquinone, and is obtained from alizarin bordeaux and *p*-toluidine and **anthraquinone green GX** is a monosulphonic acid derived from 1:4-dianilinoanthraquinone. **Alizarin saphirol** is sodium 1:5-dihydroxy-4:8-diaminoanthraquinone-2:6-disulphonate.

J. Sulphide Dyestuffs

The first dyestuffs of any importance to be manufactured were **Vidal black,** obtained in 1893 by fusing *p*-aminophenol with sulphur, and **Fast black B** from 1:8-dinitronaphthalene and sulphur. Since that time numerous yellow, brown, green, blue, and black dyes have been obtained, but so far the constitutions of these compounds have not been established. Many of them probably contain a thiazine ring.

K. Vat Dyestuffs

This is the name given to a series of insoluble dyestuffs which can be reduced to alkali soluble leuco-compounds. Many of the leuco-compounds are now sent out in stable solid forms, *e.g.* seledon colours. The fabric is immersed in the solution of the leuco compound, which is then oxidized, usually by atmospheric oxygen, to the dyestuff on the fibre. They contain the $:CO$ or $:CS$, which yield $:CH{\cdot}OH$ or $:CH{\cdot}SH$ on reduction.

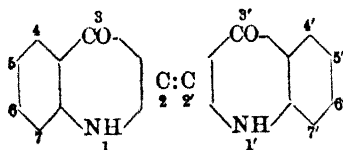
The three main sub-groups are:

1. Indigoid vat dyestuffs.
2. Anthraquinone vat dyestuffs.
3. Sulphurized vat dyestuffs.

1. INDIGOID VAT DYESTUFFS

The best known of these is indigo itself, and this has been dealt with in Chap. XXXV, p. 559. From many points of view the indigo question is one of interest to chemists. Within recent years the natural product has replaced, to a large extent, the natural dye. This is clear from the fact that the acreage under cultivation in India had fallen from nearly 1,500,000 acres in 1893 to about 150,000 in 1914. The war revived interest in the natural product, and in 1917 about 750,000 acres were under cultivation, but this acreage is again falling. For years the competition has been in favour of the synthetic product, largely owing to the number of experts engaged in endeavouring to improve the synthetic processes,* whereas very little attention had been devoted before 1916 to improvements in the cultivation of the indigo plant or the extraction of the dye. It may be accepted that the natural dye will never replace completely the synthetic product, and it is doubtful if the Indian industry will ever attain its former importance. According to *H. E. Armstrong*, the synthetic dye is inferior in dyeing properties to the natural product, due to the presence of other dyes in the latter.

For reference the following system of numbering is used:—



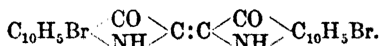
By direct bromination it is possible to replace from one to 6 atoms of hydrogen in the following order: 5, 5′, 7, 7′, 4, 4′. 6:6′-Dibromoindigo, obtained from 4-bromo-2-aminobenzoic acid is identical with one of the constituents of the ancient **Tyrian purple.** Chloro-derivatives may be prepared from chlorinated phenylglycine-carboxylic acids. The halogenated indigos are brighter and much faster to bleaching agents than indigo itself. **Ciba blue 2 B,** or 5:5′:7:7′-tetrabromoindigo is a dye of considerable commercial importance.

Indigo derivatives can be synthesised by condensing isatin

* Cf. Chap. XII in Gardner's *The British Coal Tar Industry.*

with compounds containing reactive methylene groups, *e.g.* benzocoumarone.

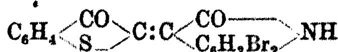
The corresponding naphthalene homologues of indigo can be synthesised from α- and β-naphthylamines by the chloroacetic acid method. They are somewhat fugitive green dyestuffs; the β-compound when brominated gives a dibromo derivative known as **Ciba green,**



Indigo yellow 3 G is indigo in which the two hydrogen atoms in the 1:1′ positions have become replaced by the bivalent benzylidene group, $C_6H_5 \cdot CH:$, and is obtained by the action of benzyl chloride in nitrobenzene solution and in presence of copper powder; it is important, as when used in the same vat with indigo it gives uniform shades of green.

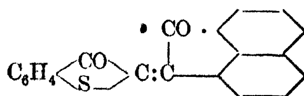
The **thioindigos** are compounds of commercial importance (*Friedlander*, 1905). **Thioindigo red,** or 2:2 bisthio-naphthene-indigo, in which the two NH groups of indigo are replaced by S atoms, is synthesised from thiosalicylic acid, $HS \cdot C_6H_4 \cdot CO_2H$, and sodium chloroacetate (cf. *Heumann* synthesis, p. 561). The first product is sodium phenylthiogylcol-*o*-carboxylic acid, which loses water and carbon dioxide, yielding hydroxy-thionaphthene, $C_6H_4 \langle {S \atop C(OH)} \rangle CH$, from which thioindigo red is obtained by oxidation with potassium ferricyanide. Numerous halogenated, alkylated, and amino-derivatives of this compound have been prepared. An interesting synthesis of thioindigo red is by condensing acetylene dichloride with sodium thiosalicylate to acetylene-bis-thiosalicylic acid, $CO_2Na \cdot C_6H_4 \cdot S \cdot CH:CH \cdot S \cdot C_6H_4 \cdot CO_2H$, which readily loses water yielding the dye (*Münch*, Z. Angew. 1907, **21,** 2059). Corresponding derivatives of the naphthalene series are also known.

An important member is **Ciba red G** or **Thioindigo scarlet G,** 2′-thionaphthene-5:7-dibromo-3-indolindigo,



and is obtained by condensing isatin with α-hydroxythionaphthene and brominating.

Ciba scarlet G is 2′-thionaphthene-acenaphthene indigo and



is obtained by condensing acenaphthaquinone with hydroxy-thionaphthene.

2. ANTHRAQUINONE VAT DYESTUFFS

These are complex derivatives of anthraquinone, and can be reduced to alkali soluble leuco compounds corresponding with oxanthranol,

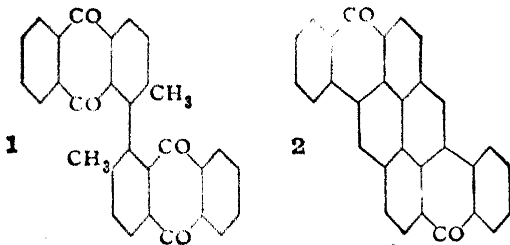


and these on exposure to the air are oxidized back to the dyes.

Anthraflavine G,

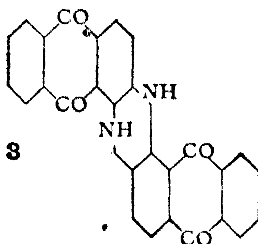


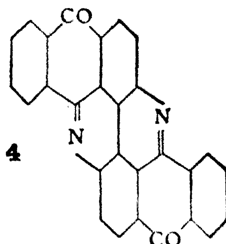
is one of the simplest members of this group, and is obtained by heating β-methylanthraquinone with alcoholic potash at 150–170°. It dyes cotton a fast greenish-yellow. **Indanthrene golden orange,** or pyranthrene, obtained by heating 2:2′-dimethyl-1:1′-dianthraquinoyl (1) has the formula (2):



Indanthrene blue R, one of the oldest and most important members of this group, is manufactured by heating β-amino-anthraquinone with potassium hydroxide and nitrate, and has the formula (3). When a higher temperature is used **Indan-**

threne yellow G, or flavanthrene, formula (4), is obtained, and yields a blue reduction product.





Algol blue K is the N-dimethyl derivative of indanthrene blue and **Indanthrene bordeaux B** is dichlorodiquinoyl-2:7-diaminoanthraquinone, $C_6H_3Cl(C_2O_2)C_6H_3 \cdot NH \cdot C_6H_3(C_2O_2) \cdot C_6H_3 \cdot NH \cdot C_6H_3(C_2O_2) \cdot C_6H_3Cl$.

3. SULPHURIZED VAT DYESTUFFS

These are obtained by heating anthracene and its derivatives at high temperatures, and are all compounds of unknown constitution.

Hydron blue R is a very common cotton vat dye, and is manufactured from carbazolindophenol and sodium polysulphide.

LVI. THE CHEMISTRY OF RUBBER

In the domain of organic chemistry few subjects afford a better illustration of the interplay of scientific, technical, and commercial factors in the development of an industry than rubber does.

The importance of the rubber industry can be gathered from the fact that even in 1911 it represented an annual value of about £45,000,000 or roughly twice the value of the synthetic dyestuffs industry. The production for 1929 was 850,000 tons at an average selling price of £95·5 per ton, or a value of £81,000,000.

Rubber is manufactured from the milky-white, sticky juice or latex produced when certain species of trees, shrubs, and creepers are tapped or cut.

The three stages in the production of commercial rubber are:—[*]

1. The collection of the latex; 2, the coagulation of the latex, and the production of raw rubber or caoutchouc; and 3, the curing or vulcanization of the raw rubber.

A. Sources of Rubber. The Latex. Coagulation.

Sources of Rubber.—The chief rubber-producing countries are: South America, notably the regions of the Amazon and Para, East and West Africa, the Malabar Coast of South India, Burma, Ceylon, the Malay Peninsula, Siam, and Cochin China. In South America the latex is obtained from species of **Hevea,** more particularly *H. Siberi* and *H. braziliensis*, a good specimen of which will yield as much as 22 lb. of rubber per annum.

The trees are all of wild growth, and are tapped in the early morning, when the yield of latex is high, by making incisions with a small iron hatchet, the first tapping being made about two metres from the ground. The latex is caught in small tin-plate cups; the tapping is continued for a week, each morning fresh incisions being made lower down the stem (some 25 cm.), and the cups moved to different positions. At

[*] Cf. *Fisher*, Chem. Rev. 1930, 51.

the end of the week the latex is removed, and, after a process of rough filtration, coagulated by exposure in a thin stream to the dense smoke obtained by burning resinous woods. Rubber is also obtained from *Castilloa costaricana* in Mexico and South America, but the yield is only about 4–5 oz. of rubber per tree per annum. A third South American source of rubber is the shrub *Parthenium argentatum*, which is harvested, and the latex separated mechanically from the tissue; the product is known as "Guayle rubber" (I. R. World, 1928, **79**, 53).

In tropical Africa numerous creepers, herbaceous plants, and trees yield latex, and are used as sources of rubber, the method of extraction varying with the nature of the source. Some of the older methods were based on the chopping down of all plants in a given area, a method which would rapidly lead to the exhaustion of supplies. The different governments concerned are endeavouring to replace such methods by more scientific ones. As a rule the African plants are not suited to the process of tapping, and the cutting down of certain marked plants or trees, without interfering with the roots, is being adopted, new supplies being secured by new growths combined with restocking. In most cases a mechanical method of separating the latex is necessary.

In Asia the whole of the rubber is derived from plantations and not from indigenous forests. Extensive plantations were laid down by the British in 1876 in Ceylon and the Federated Malay States, by the Dutch in 1882 in Java, Sumatra, Borneo, and in 1885 by the French in Tonkin, Cambodia, and Laos. The majority of the plantations consist of *Hevea*, which are propagated by seeds, or more frequently by cuttings. The trees begin to yield rubber in workable quantities when six to ten years old; at first they are tapped every other year, but when mature can be tapped every year, usually after the rainy season, and never during the period of flowering. The yield of rubber from a mature tree is about 3·5 to 4·5 lb. per annum.

During the years 1908–17 rubber production in the Amazon district has remained practically stationary at about 38,000 tons a year, whereas the figures for plantation rubber have increased from 2200 tons in 1908 to 210,000 tons in 1918 and 813,000 tons in 1929, and 70 to 80 per cent of the total supply is produced within the British Empire. The statistics for 1918 are:—

plantation para, 210,000,* South American wild para, 38,000, and other sorts, 12,000 tons.

As plantation rubber is practically dry, and even hard Para rubber contains 20 per cent of moisture, 80 to 90 per cent of the total world's supply of rubber is derived from plantations.

It is generally admitted that the South American and African sources have reached their zenith, and that the production is not likely to increase in the near future.

The enormous increase in the production of plantation rubber is largely due to the scientific management, the relatively low costs of production, and the better transport facilities as compared with South America.

The cost of production has fallen from about 10*d*. per pound in 1915 to 7*d*. per pound in 1922, and finally to about 4*d*. per pound in 1930. The big increase in production between 1925–29 has resulted in a big fall in selling price, viz. from over 4*s*. per pound in 1923 to about 4*d*. per pound in 1930, as so far the demand has not kept pace with the increased supply.

As a rule the plantation trees are not so hardy as wild trees, and too drastic tapping lowers their vitality, and renders them liable to suffer from parasitic diseases, and also from attacks by " white ants ".

Attempts to cultivate species of *Castilloa* and Manihot (*Ceara*) have been made, but have not met with the same success as Hevea plantations, and the general tendency is for the disappearance from commerce of rubber derived from botanical sources other than Hevea. The raw rubber obtained from Hevea, Castilloa, and Manihot is rich in caoutchouc and poor in resins (2-7 per cent). Within recent years attention has been drawn to low-grade rubbers rich in resins.† The most important of these is " Jetulong " or " Dead Borneo ", derived from *Alstonia costulata* (Miques), and *Dycra costulata* (Hooker). It contains 40–50 per cent of water, 30–40 per cent of resins soluble in acetone, and 15–20 per cent of caoutchouc. After removal of the resins by extraction it yields a rubber which is said to be of excellent quality, and the extracted resins themselves also find commercial uses.

The Latex.—The latex of Hevea is a white liquid with the

* For 1920, 340,000 tons.

† The resins are soluble in absolute alcohol or acetone, whereas caoutchouc is not.

consistency of cows' milk, and is more or less sticky according to the amount of rubber it contains, a factor which also appreciably affects its specific gravity. The latex appears to be an emulsion of rubber in water which holds in suspense or solution glucosides, sugars, resins, proteins, enzymes, organic acids, and mineral salts. The composition varies within wide limits according to the botanical source, the age of the plant, the season, the method of production, and the height above ground at which tapping occurs. Cf. *de Vries*, Comm. Central Rubber Stat. Brutzenzorg, Java, 1918, **2**, 241; 1919, **3**, 128, 137, 207; *Whitby*, Ind. J. 1919, **58**, 895. The percentage of rubber tends to increase with the age of the tree (as a rule trees should not be tapped until they are 6–10 years old), and to diminish with the height of the tap hole from the ground.

The following may be taken as typical analyses of Hevea latex:—

	Amazon Delta.	Ceylon Plantation.
Water	47·0	55·2
Caoutchouc	32·0	41·3
Mineral salts	9·7	0·4
Proteins	2·3	2·2
Resins	9·0	2·0
Sugars	—	0·4

Nearly all latices contain small amounts of sugars and glucosides. Most of the sugars appear to be related to inositol (p. 450), and not to the glucose group. The substance known as **Dambonite,** $C_8H_{10}O_6$, and present in most latices appears to be an inositol dimethyl ether, $C_6H_6(OH)_4(OCH_3)_2$. *l*-Inositol monomethyl ether is also present in Hevea latex (*Pickles* and *Whitfeild*, Proc. Chem. Soc., 1911, **27**, 54).

Many latices are alkaline to litmus when freshly tapped, but when kept they undergo bacterial fermentation producing organic acids, mainly lactic, which bring about coagulation. The latices from species of Ficus are acid, the acidity being due to a peculiar organic acid, the sodium and potassium salts of which are insoluble. Oxidases are usually present, and when exposed to the air the latex tends to turn brown. The addition of a little sodium bisulphite prevents this darkening without impairing the properties of the rubber. Anti-oxidants, probably unsaturated sterols, are also present (Ind. Eng. Chem. 1927, 1187).

The suggestions which have been made as to the function

of the latex in the plant are: 1, a reservoir of nutritive material in the plant; 2, a waste product; 3, a protective material produced by the plant to assist in healing wounds, and to protect the plant against insect attacks. The real function of Hevea latex is multiple in character. It serves as a reservoir of nutritive substances and of water; it is a medium for the transportation of materials necessary for the growth of the plants, and also possesses protective properties.

There is an increasing tendency to use latex direct for the manufacture of rubber goods. This means the preservation of the latex for export and in many cases its partial concentration in order to reduce transport charges. The preservative generally used is ammonia or an organic amine, or sometimes an organic antiseptic and trisodium phosphate. The methods of concentrating are (*a*) the preserved latex is allowed to stand when a cream rises; (*b*) the preserved latex is centrifuged or (*c*) creaming reagents, such as Irish moss or gelatine, are added. Such creams contain roughly 75 per cent of rubber hydrocarbons and are free from the water soluble non-rubber constituents of the latex. Concentration is also possible by the addition of a stabiliser, *e.g.* aqueous potassium hydroxide, potassium fluoride or salicylate and evaporation under diminished pressure. The creams are sometimes butter-like in consistency, but can be readily diluted with water. Such latex can be used direct for the electrodeposition of rubber, or rubber mixed with different ingredients, on a zinc or other anode. Latex or concentrated latex can be vulcanized in the same way as raw rubber, and it is claimed that rubber obtained direct by electrodeposition is more durable than ordinary rubber.

At the present time the latex is used for the manufacture of the following articles: Tire-web cord fabrics, gloves, inner tubes, rubber impregnated mohair fabrics, special papers and rubber-covered metallic articles (by electrodeposition).

Coagulation.—Three methods of coagulation are used, viz.:—

1. The smoking process adopted in the Amazonian district, and already mentioned (p. 946). This process consists partly in the coagulation of the rubber by the rapid evaporation of the serum as it is exposed in a thin layer to hot smoke, partly in the coagulation by the acids present in the smoke, viz. carbonic, formic, and acetic, and preservation of the rubber from decomposition by the creosote contained in the tar.

The process consists in allowing the latex to flow slowly on to a large wooden paddle, which is slowly rotated by hand in the dense smoke. The process is continued until 20–100 lb. of rubber have been built up on the paddle, and this constitutes the "fine Para" of commerce. Types of smoking machines have also been introduced.

2. *The Acid Process.*—The great bulk of the plantation latex is usually coagulated by acetic acid. Other acids or acidic substances can also be used, for example, formic, lactic, sulphuric acids, sodium hydrogen sulphate, alum, sulphurous acid, &c. During the war the difficulty of obtaining acetic acid led the rubber makers to use several of these. This process of coagulation necessitates careful washing of the raw rubber in order to remove the acid. The quantity of acetic acid used is usually 1–2 per cent of glacial acid calculated on the latex, but can be varied within fairly wide limits. The addition of too much is harmful, as the rubber obtained does not cure so readily. In actual practice the amount of acetic acid added for coagulation is usually insufficient to produce coagulation by itself, and the view now generally held is that the coagulation is due to an enzyme which is activated by the addition of acid, and that the process is somewhat analogous to the setting of milk by rennet (*Barrowcliff*, J. S. C. I. 1918, **37**, 48 T.).

The addition of a large amount of acid destroys the enzyme, and the coagulation is then due to the action of the acid on the negative suspensoid.

3. *Auto-coagulation.*—When the latex is mixed with about 0·2 per cent of glucose and kept, coagulation due to non-putrefactive bacterial action occurs, and is complete in eighteen hours. The coagulum has a sweet odour, whereas in the absence of glucose putrefactive bacteria tend to develop, and the coagulum acquires a disgusting odour. If air is excluded the coagulation is not complete. This method is used in the Malay Peninsula, and may in time replace the acid process.

Various statements have been made with reference to the relative values of Para and plantation rubber. It has been stated that the washing necessary in the acid coagulation process impairs the value of the rubber. Others state that plantation rubber is as good as, or even better than, Brazil Para (compare J. Ind. 1915, **34**, 989; 1916, **35**, 263, 493, 1715; 1918, **37**, 237 R., 95 T., 48 T., 262 T.). It is usually

free from dirt which is found in Para rubber. At any rate, "fine Para" fetches a higher price than plantation rubber on the market. One drawback of plantation rubber is that it usually does not vulcanize so readily (see, however, p. 972, and compare *Whitby*, J. Ind. 1916, **35**, 493). In Ceylon and elsewhere the raw rubber produced by the acid coagulation process is subsequently smoked. For variability of plantation rubber, cf. *Eaton*, *Grantham*, and *Day* (Ag. Bull. F. M. S. 1918, **27**, 1).

Theories of Coagulation.—*Weber's* views on coagulation are that the process is entirely dependent on the presence of coagulable proteins in the latex, and thus the process of coagulation is strictly comparable with the clarification of wines or beer by means of gelatine. It follows that the coagulation of the latex can be effected by means of any of the precipitants of albumen, and that the rate of coagulation is a function of the nature of the albuminoids and of the amount of inorganic matter present in the serum. Substances which interact vigorously with proteins produce instantaneous coagulation. *Gardner*, on the other hand, claims that proteins are not indispensable for coagulation; by digesting the proteins with papain, and removing the products of digestion by dialysis he obtained a protein-free latex which could be coagulated by pouring into absolute alcohol. The proteins probably function as emulsifying agents and keep the oily drops in the serum; the membrane enveloping the rubber globules does not consist of protein, as it resists the action of papain. *V. Henri* claims that rubber latex is an ordinary negative colloid, and behaves as such when the mineral salts are removed by dialysis. In the latex the globules are negatively charged with respect to the liquid or serum in which they are suspended, and, as in other cases of negative emulsions, the precipitation can be effected by means of small amounts of acids, or by salts of the bi- and tervalent metals irrespective of the acid radical.

These views are now generally accepted, and the latex is regarded as a milky fluid containing minute globules of a colloid (*Hinrichsen* and *Kindscher*, J. Ind. 1910, **29**, 34), probably rubber itself, in a state of colloidal suspension in an aqueous fluid. In Hevea latex the globules are microscopic and show Brownian movements. It is a negative suspensoid and behaves as such; acids produce coagulation or precipita-

tion, and alkalis increase the stability of the suspension. The protein content of the latex increases the stability of the suspensoid, the dissolved protein or peptone acting as a protective colloid.

A view held by some chemists is that coagulation in both processes is due to an enzyme, and that the function of the added acid is to activate the enzyme present in the latex (*Barrowcliff*, J. Ind. 1918, **37**, 48 T., 262 T.; *Whitby*, Ag. Bull. F. M. S. 1918, **6**, 374); other chemists (ibid. 1915, **4**, 28; 1917, **5**, 48; J. Ind. 1918, 631 A.) hold that in the auto-coagulation process the activity is due to bacterial agency.

If the latex is freed from saline matter by dialysis through a collodion film, salts of univalent metals have practically no effect, salts of bivalent metals produce coagulation at any concentration above normal, and salts of tervalent metals at concentration greater than 0·05 N. Acids produce the same effect at concentration of 0·5 N. (*V. Henri*, C. R. 1907, **144**, 431.)

B. Raw Rubber or Caoutchouc

The clots formed during coagulation consist of separate particles united to form a tenacious elastic network, and the structure of the clot varies with the coagulant used. Weak coagulants produce a network with an open mesh and slight elasticity, whereas strong coagulants produce a close mesh and a clot of high elasticity.

Like most gels, rubber itself is an emulsoid consisting of the colloid hydrocarbon rubber $(C_{10}H_{16})_n$ in a fine state of dispersion in a colloidal medium, consisting partly of protein, but mainly of a modification of rubber. Thus rubber not only forms the disperse phase, but also its own dispersion medium.

During the process of coagulation a portion of the resins, proteins, and mineral salts are precipitated with the rubber. Para rubber contains much larger quantities of these impurities than plantation, and the presence of some of the nitrogenous substances is advantageous as it facilitates the subsequent process of curing.

Most of these impurities can be removed by dissolving the rubber in a suitable solvent. As in the case of most gels, the solution is preceded by a process of swelling or adsorption

of solvent, and, finally, a colloidal solution of high viscosity is obtained which is difficult to filter. Benzene can be used in this way, and if a little trichloracetic acid is added subsequently the solution becomes limpid, and can be easily separated from the impurities. Carbon disulphide, benzene, and chloroform yield almost transparent clear solutions, whereas ether and petroleum ether yield turbid liquids. The turbidity is due to the fact that the rubber is not so soluble in these solvents, and the insoluble part exists in a finely dispersed form throughout the solution. Even the apparently clear benzene solutions exhibit discontinuity under the ultra-microscope. In a similar manner, if a 2 per cent solution of rubber in light petroleum is exposed for three minutes to ultra-violet rays from a Westinghouse lamp, a limpid solution is obtained.

Para rubber contains about 6 per cent of insoluble matter rich in oxygen, and consisting of (*a*) intermediate products in the formation of rubber; (*b*) oxygenated derivatives of rubber; (*c*) highly-polymerized hydrocarbons; (*d*) proteins; (*e*) enzymes, such as oxidases, which can produce discoloration of the rubber.

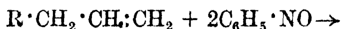
The impurities, *e.g.* resins and proteins, present in the raw rubber are not removed in practice, as the expense would be great, and as it has been found that the resins tend to prevent the oxidation of the rubber, and the proteins accelerate the process of vulcanization.

The soluble portion consists of a hydrocarbon $(C_{10}H_{16})_n$, but usually contains combined oxygen, *e.g.* 0·61 per cent in Para.

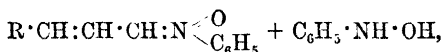
The following are the most characteristic derivatives which caoutchouc forms. A **tetrabromide,** $C_{10}H_{16}Br_4$ (*Gladstone* and *Hibbert*, *Weber*) which has no definite melting-point but decomposes when heated. An **iodide,** $C_{10}H_{16}I_3$ (*Weber*), in the form of a brown powder decomposed by light or heat. A **dihydrochloride,** $C_{10}H_{18}Cl_2$. A **monohydriodide,** $C_{10}H_{17}I$ (B. 1913, **46,** 1283). The product obtained by the removal of halogen hydracids from these compounds by means of bases is not identical with the original caoutchouc, and is termed *a*-isocaoutchouc (B, 1913, **46,** 736). A **nitrosite** $(C_{10}H_{16}N_2O_3)_n$ (*Harries*, B. 1900, **33,** 779), obtained by passing dry nitrous anhydride fumes into a benzene solution of pure rubber, is a friable, greenish solid, insoluble in most solvents, and has no definite melting-point. A **nitrosite,** $C_{20}H_{30}O_{14}N_6$, obtained by

passing moist nitrous gases into a benzene solution of rubber; it decomposes at 158°–162°, and is used in estimating rubber. An **ozonide**, $C_{10}H_{16}O_6$, obtained by passing purified ozonized air into a 1 per cent chloroform solution of rubber (*Harries*, B. 1904, **37**, 2708; 1912, **45**, 936), evaporating to dryness at 20°, dissolving in ethyl acetate, and precipitating with petroleum ether. It forms an explosive vitreous mass, melting at 50°, and is soluble in most solvents.

The rubber molecule also reacts with nitrosobenzene in much the same manner as olefines do, yielding a **nitrone**, *e.g.*



$$R\cdot CH_2\cdot CH{:}CH_2 + 2C_6H_5\cdot NO \rightarrow$$



$$R\cdot CH{:}CH\cdot CH{:}N\langle{}^{O}_{C_6H_5} + C_6H_5\cdot NH\cdot OH,$$

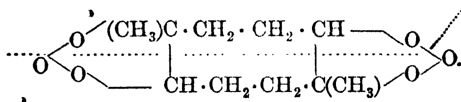
accompanied by a shifting of the olefine linking.

The empirical formula deduced from analysis is C_5H_8, and the formation of the derivatives already described indicates that the simplest formula is $C_{10}H_{16}$ with two olefine linkings in the molecule, as the smallest molecular weight for the ozonide, determined by the cryoscopic and ebulliscopic methods, is 230. The general properties indicate a much more complex molecule, but as the molecular weight cannot be determined, the value of *n* in the formula $(C_{10}H_{16})_n$ is uncertain, but is usually accepted at 6–8. At temperatures up to 180° the complex $C_{10}H_{16}$ is still retained, although the ordinary physical characteristics have altered. At higher temperatures decomposition products are formed, and oily products equal in weight to 84 per cent of the rubber used are obtained. This distillate dissolves raw rubber at the ordinary temperature, and contains butylene, isoprene (p. 611), a terpene hydrocarbon, caoutchine (boiling at 176°–180°, and since proved to be dipentene), and a sesquiterpene, **hevene**, boiling at 255°–265° (*G. Williams*, 1860, and *G. Bouchardat*, Bull. 1875, **24**, 108).

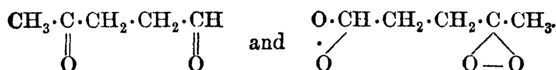
Constitution of Caoutchouc.—The constitution is largely based upon the following considerations:—(*a*) the close relationship between isoprene and rubber; (*b*) the formation of the additive compounds mentioned above; and (*c*) a study of the decomposition products of the ozonide.

Tilden (Chem. News, 1882, **46**, 220), who prepared isoprene by breaking down pinene and dipentene, was the first to suggest the constitution of isoprene as 2-methyl-$\Delta^{1:3}$-butadiene (p. 611),

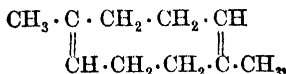
a conclusion which has since been confirmed by various syntheses. As isoprene yields caoutchouc under the influence of heat or of small amounts of various chemicals, the latter would appear to be a polymer of isoprene. Its reactions with bromine, hydrogen chloride, nitrogen peroxide, and ozone indicate the presence of two olefine linkings in each $C_{10}H_{16}$ portion of the molecule. When the ozonide is decomposed by boiling water the products are lævulic aldehyde, $CH_3 \cdot CO \cdot CH_2 \cdot CH_2 \cdot CHO$, and lævulic aldehyde peroxide, which yields lævulic acid (p. 238), and hydrogen peroxide. It is claimed by *Harries* that these facts are most readily explicable if the ozonide is represented as containing a cyclic nucleus with an 8-membered carbon ring, *e.g.*



The rupture takes place as represented by the dotted line, and the products are lævulic aldehyde and lævulic aldehyde peroxide:



The decomposition is thus analogous to that of other ozonides derived from olefine compounds (p. 694), and the original hydrocarbon from which the ozonide was derived must be 2:6-dimethyl-cyclo-Δ1:5-octadiene:

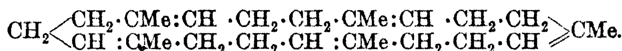


and the caoutchouc molecule a polymeride of this.

This rubber unit, $C_{10}H_{16}$, is extremely interesting as being a representative of an 8-membered carbon ring, the saturated parent substance of which is octamethylene or cyclo-octane, $CH_2<\begin{smallmatrix}CH_2 \cdot CH_2 \cdot CH_2\\CH_2 \cdot CH_2 \cdot CH_2\end{smallmatrix}>CH_2$ (compare Polymethylenes, Chap. XVI). Numerous derivatives of this are known. One of these is the cyclic ketone, **azelaone**, $CH_2<\begin{smallmatrix}CH_2 \cdot CH_2 \cdot CH_2\\CH_2 \cdot CH_2 \cdot CH_2\end{smallmatrix}>CO$.

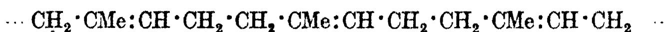
This ring structure of the rubber unit is not generally accepted. It is difficult to account for the polymerization of the units without destroying their identity. There is no evidence of the formation of such ring compounds when rubber is decomposed, and the known octadienes polymerize giving crystalline products entirely different from rubber.

Harries (A. 1914, **406**, 173) has modified his views, and now regards the unit of the caoutchouc molecule as $(C_5H_8)_5$ or $C_{25}H_{40}$:



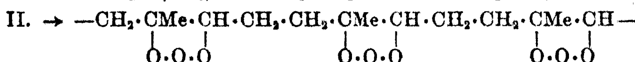
This change is mainly due to the fact that α-isocaoutchouc (p. 969) yields an ozonide which on decomposition gives rise to the following compounds:—lævulic aldehyde; diacetylpropane, $CH_3·CO·[CH_2]_3·CO·CH_3$; undekatrione, $CH_3·CO·[CH_2]_3·CO·[CH_2]_3·CO·CH_3$; pentadekatrione, $CH_3·CO·[CH_2]_3·CO·[CH_2]_3·CO·[CH_2]_3·CO·CH_3$, and the corresponding acids. The caoutchouc ring is thus represented as built up of 20 carbon atoms with 5 methyl substituents and 5 olefine linkings.

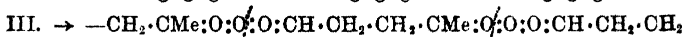
Weber, *Pickles* (J. C. S. 1910, **97**, 1088), and others consider the caoutchouc complex is a long chain built up from C_5H_8 groups by normal polymerization, and with the two ends joined to form a closed ring, *e.g.*



The number of the C_5H_8 groups is uncertain, but *Pickles* suggests at least 8. In this polymerization a shifting of olefine linkings has taken place, and the formation and decomposition of the ozonide can be accounted for as follows:—A molecule of ozone is added on at each olefine linking







The union between the carbon atoms is then ruptured, so that the ozonide has the structure No. III, which is decomposed by water into lævulic aldehyde and the corresponding peroxide as indicated by dotted lines (cf. *Ostromisslenski*, J. Russ. 1915, 1932).

Boswell (Can. Chem. 1922, 238) has suggested a different

type of condensation of the isoprene molecules, the olefine linkings of 3 molecules reacting to give first a compound of the type of a trimethyl-dicyclohexene with one olefine linking in each ring, and in virtue of these further condensation with isoprene molecules takes place, *e.g.* three yielding a complex cyclic structure $C_{30}H_{48}$. On degradation with hydrogen peroxide it yields compounds of the type $C_{26}H_{42}O_2$, $C_{20}H_{40}O_9$, and $C_{15}H_{24}O$. Such a formula does not readily account for the formation of ozonides. X-ray studies indicate that the rubber hydrocarbon consists of long chains of isoprene groups and that these chains probably exist as spirals which form definitely alligned fibres when the rubber is stretched.

C. Synthetic Rubber

In all synthetic processes for the production of rubber there are the two distinct stages, viz.: (1) the preparation of isoprene, or of a homologue containing the conjugate linking, .. C:CH·CH:C ...; (2) the polymerization of this hydrocarbon to rubber.

The pure chemist regards the actual synthesis as the final argument in favour of a particular constitution of the compound based on analytical reactions. This point of view is also of interest in discussing the structure of isoprene and indirectly of rubber. The view put forward by *Tilden* in 1882 that isoprene is 2-methyl-$\Delta^{1:3}$ butadiene, CH_2:CMe·CH:CH_2, has since been confirmed by various syntheses. The technical chemist, on the other hand, is apt to regard a synthesis from the commercial point of view, and his object is to obtain a laboratory method of producing the compound which will enable the manufacturer to put the artificial product on the market at a price which will compete with the product obtained from natural sources. The numerous processes which have been described within the last few years for preparing isoprene, its homologues and analogues, have, in most cases, been worked at with this object in view. It is clear that, in order to put on the market an artificial rubber, which shall compete successfully with plantation rubber, the cost of producing which has been reduced to about fourpence per pound, the following conditions must be fulfilled:—

1. The raw material used must be available in sufficient quantity, and at a sufficiently low price. In many of the

methods of making isoprene starch has been used as the raw material. There is an abundance of this material, but as the prices of all cereals have appreciated in value within the past few years, the possibility of the successful solution of the synthetic rubber industry appears to be as remote as ever. Similar statements hold good for coal-tar products and low boiling petroleum fractions.

2. The materials used in the various stages of the synthesis must also be relatively cheap, and the use of sodium, methyl iodide, bromine, &c., is impossible.

3. The number of intermediate stages should be few.

4. The yields of the intermediate products obtained in the different stages must be good. Cf. *J. B. Farmer*, J. R. S. A. 1918, **66**, 490; *Duisberg*, Z. Elec., 1918, **24**, 369; J. I. E. C., 1919, **11**, 819.

It is improbable that any of the methods mentioned on pp. 963–966 can yield a synthetic product which can compete with natural rubber at fourpence per pound; but if the price should rise to 1 shilling to 2 shillings per pound owing to increased demands, the question of synthetic rubber would again become a commercial proposition.

An important question in connexion with artificial rubber is the identity of the natural and synthetic products. The natural rubber molecule contains the complex $(C_{10}H_{16})_n$, or several such complexes. It might be possible to build up a synthetic product in which the $C_{10}H_{16}$ unit was the same as in the natural product but with a formula $(C_{10}H_{16})_n$. Further possibilities are that the $C_{10}H_{16}$ unit is isomeric, and not identical with the $C_{10}H_{16}$ unit in natural rubber, and lastly, the possibility of substituting a homologous group, C_8H_{12}, C_9H_{14}, or $C_{11}H_{18}$ for $C_{10}H_{16}$. The possibilities of realizing such syntheses are obvious when it is remembered that the process of polymerization is characteristic not only of isoprene but of all analogous hydrocarbons containing the conjugate olefine linking, $\overset{1}{C}:\overset{2}{C}\cdot\overset{3}{C}:\overset{4}{C}$. Examples of such compounds are:—

1. Butadiene or erythrene, $CH_2:CH\cdot CH:CH_2$; 1:3-Pentadiene or piperylene, $CH:CH\cdot CH:CH\cdot CH_3$.

2. 2:3-Dimethylbutadiene or methylisoprene, $CH_2:CMe\cdot CMe:CH_2$ (*Kondokoff*, J. pr. 1901 [ii], **64**, 109).

3. 1-Phenylbutadiene, $C_6H_5\cdot CH:CH\cdot CH:CH_2$ (*Klages*, B. 1902, **35**, 2649).

4. 1-Bromobutadiene, $CHBr:CH\cdot CH:CH_2$ (*Willstätter* and *Bruce*, B. 1907, **40**, 3979).

5. Dihydrotoluene, methylcyclohexadiene (*Harries*, B. 1901, **34**, 300).

6. Cyclopentadiene, $CH\begin{cases} CH\cdot CH \\ \quad\ \ \| \\ CH_2\cdot CH \end{cases}$ (*Kronstein*, B. 1902, **35**, 4151).

According to *Lebedeff*, in hydrocarbons containing a conjugate ethylene linking the velocity of polymerization is greatest when the atoms 1 and 4 in the system are heavily and the atoms 2 and 3 less heavily laden.

The condensation products of many of these compounds are sticky masses of no value as rubber substitutes; others, *e.g.* butadiene yield products which are somewhat difficult to distinguish from natural rubber.

Formation of Isoprene and its homologues.—For summary of methods cf. *Ostromisslenski*, J. Russ. 1915, **47**, 1472, Abs. 1916, i, 2.

Methods of Theoretical Importance

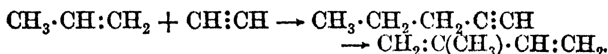
1. Methods of destructive distillation.

By distilling rubber under atmospheric pressure *Weber* obtained 6·2 per cent of isoprene, 46 per cent of dipentene, and 26·8 per cent of polyterpenes. *Fischer* and *Harries* working under a pressure of 0·25 mm., obtained only small yields of isoprene and dipentene. In 1884 *Tilden* prepared small amounts of isoprene by passing the vapour of pinene or dipentene through an iron tube at a dull red heat. According to *Ipatieff* the optimum temperature is 270°–280°. Myrcene and sylvestrene also yield isoprene, but terpinolene, carvestrene, terpinene, and camphene do not (compare formulæ, pp. 620, 621, 630). *Harries* and *Gottlob* (A. 1911, **383**, 228) obtained a 40 per cent yield of isoprene by allowing the vapour of dipentene to come in contact with a platinum wire 120 cm. long, and with a resistance of 90 ohms, at a moderate red heat. By means of a condenser the undecomposed terpene is made to flow back into the original vessel, whereas the isoprene vapours pass on, and are subsequently condensed by means of a refrigerating plant. The yield can be raised to about 60 per cent by working under a pressure of 2–3 mm. (*Standinger* and *Klever*, B. 1911, **44**, 2212).

Sulphur dioxide is frequently used for purifying isoprene or butadiene. Liquid sulphur dioxide completely absorbs either compound, and they can be isolated by distillation. Another method is to pass sulphur dioxide gas into an acetone solution of the impure hydrocarbon, when a white precipitate is formed.

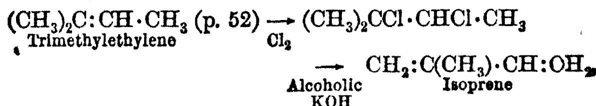
2. From methane.

By passing methane over carbon impregnated with copper oxide, and heated to 400°–450°, a 42 per cent yield of propylene, together with ethylene (36 per cent) and higher olefines and hydrogen, is obtained. The propylene is mixed with acetylene, and passed over animal charcoal at 150°, the first product is *n*-propylacetylene, and this changes into isoprene.



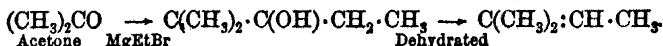
The ethylene can react in a similar manner with acetylene yielding ethylacetylene, which is isomerized to butadiene when passed over pumice heated at 300°.

3. From amyl alcohol, as represented by the following scheme (*Kondakoff*):—

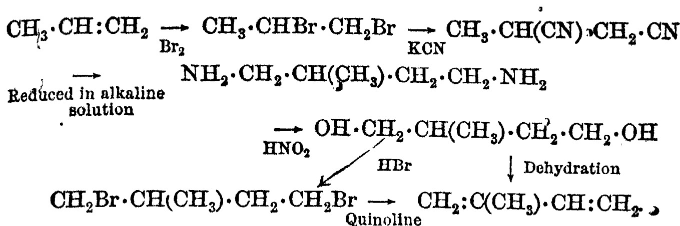


the yield is about 7 per cent of the weight of the trimethylethylene used.

The dibromide of trimethylethylene when heated with soda lime yields isoprene, but with alcoholic potash gives dimethylallene. Numerous methods of obtaining trimethylethylene and its dibromide have been worked out, one of them is as follows:—



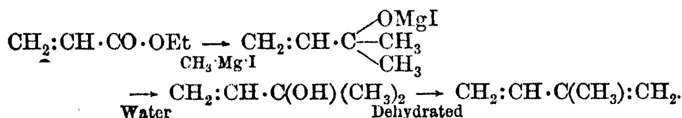
4. From propylene (*Euler*, B. 1895, **28**, 2952; 1897, **30**, 1989).



The final product is isoprene in a pure form.

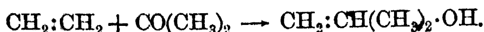
5. From 2-methyl-2:4-dibromobutane, $(CH_3)_2CBr\cdot CH_2\cdot CH_2Br$, which can be prepared by the addition of hydrogen bromide to dimethylallene, or the addition of bromine to 1:1-dimethylcyclopropane (p. 346), by the elimination of hydrogen bromide. The hydrocarbon prepared by this method is not pure, and probably contains dimethylallene, as obviously hydrogen bromide can be eliminated in two different ways.

6. From ethyl acrylate (p. 170), by *Harries* and *Neresheimer* (1906), as indicated in the following scheme:



7. From acetone and ethyl α-bromopropionate. These react with zinc according to the *Reformatsky* reaction (p. 272), yielding $(CH_3)_2C(OH)\cdot CH(CH_3)\cdot CO_2Et$, from which ethyl trimethylacrylate, $(CH_3)_2C:C(CH_3)CO_2Et$, is obtained by the elimination of water, and this in its turn, by conversion into its dibromide and heating with caustic soda, gives isoprene.

Another method of obtaining isoprene from acetone is by condensing the acetone with ethylene made from acetylene and hydrogen:

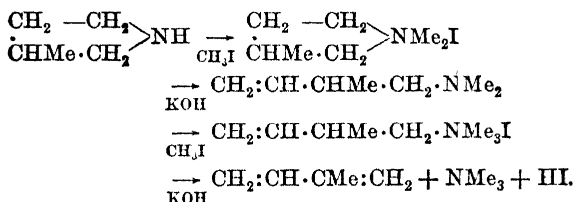


The alcohol, isopropenyl alcohol, when dehydrated, yields isoprene together with dimethylallene.

8. From amines by the process of exhaustive methylation (p. 593). This is a general method for obtaining unsaturated

compounds from amino derivatives of saturated hydrocarbons. The process consists in converting the amine into a quaternary ammonium iodide, and subsequently into the corresponding hydroxide by means of moist silver oxide, or sometimes by means of potassium hydroxide and then distilling the quaternary base.

Euler (B. 1897, **36**, 1989; J. pr. 1898 [ii], **57**, 131) obtained isoprene from β-methylpyrrolidine (p. 611) by this process. The reaction takes place in two stages, the first resulting in the rupture of the ring, and the second in the formation of the unsaturated hydrocarbon.



Pyrrolidine when treated in a similar manner gives a small yield of butadiene.

9. An interesting method of formation of $\beta\gamma$-dimethylbutadiene or methyl-isoprene, $CH_2{:}C(CH_3){\cdot}C(CH_3){:}CH_2$, is from pinacone (p. 200), and, provided acetone could be obtained in sufficient quantity and at a low price, this might prove a method adapted for commercial work. The acetone is reduced by means of magnesium amalgam, or with aluminium and alkali; according to *Holleman's* process, the magnesium amalgam is produced electrolytically in situ and acts upon the acetone in the nascent state. The yields are good and the process rapid, especially in the presence of a little mercuric chloride.

The methylisoprene is made by the action of sulphates having an acid reaction, *e.g.* alum or copper sulphate, on pinacone at 140°, or better by passing pinacone over alumina heated to 400°, when a 70 per cent yield of hydrocarbon, boiling at 69°, is obtained.

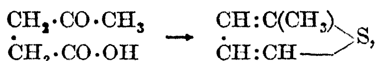
Methods which might be of Commercial Importance

1. **English Process.**—By the fractional distillation of fusel oil (pp. 79, 786) an amyl alcohol boiling at 128°–131° is obtained. This contains 87 per cent of isoamylalcohol, $(CH_3)_2CH\cdot CH_2\cdot CH_2\cdot OH$, and 13 per cent of active amyl alcohol, $CH_3\cdot CH_2\cdot CH(CH_3)\cdot CH_2\cdot OH$ (p. 84). Dry hydrogen chloride converts the alcohols into the corresponding amyl chlorides, and the fraction boiling at 97°–101° is separately collected and subjected to the action of chlorine in bright sunlight in a special apparatus, so arranged that the vapour of the boiling liquid enters a globe attached to a reflux condenser and reacts with chlorine in the globe. The reaction is stopped as soon as the thermometer immersed in the vapour registers the required temperature. The liquid is then fractionated, and the product, boiling at 140°–175°, collected separately. This fraction contains the following dichloro compounds, mainly No. 2:

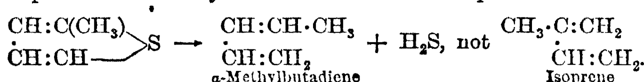
1. $(CH_3)_2CH\cdot CHCl\cdot CH_2Cl$, boiling-point 142°;
2. $(CH_3)_2CCl\cdot CH_2\cdot CH_2Cl$, boiling-point 152°;
3. $CH_2Cl\cdot CH(CH_3)\cdot CH_2\cdot CH_2Cl$, boiling-point 170°;

all of which have been isolated and their structural formulæ established (*Perkin*, J. Ind. 1912, **31**, 621). When this mixture is passed over coarse soda lime heated at 470°, and the product collected and fractionated, a 40 per cent yield of isoprene, boiling at 28°–36°, can be obtained. The chief drawback of the method is the limited amount of fusel oil available (in 1912 the estimated amount was 35,000 tons), and its comparatively high price owing to the fact that it finds application in the varnish, and other industries. Numerous investigations on the yields of amyl alcohol from different starchy materials and using different organisms have been carried out (cf. *Dubose* and *Luttringer*, Eng. trans., pp. 289–292), and numerous methods have been suggested for increasing the yields of fusel oil, more particularly of amyl alcohol during alcoholic fermentation; one of the most important of these is the addition of amino acids, more particularly the addition of material rich in leucine (p. 787), to the fermenting mass, suitable materials being the by-

under pressure appreciable quantities of lævulic acid (p. 238) are obtained. This acid reacts with phosphorus trisulphide yielding α-methylthiophene,



which can be converted into isoprene by passing the vapour mixed with hydrogen over heated copper. It is stated that each kilo of starch will yield 112 grammes of caoutchouc. According to *Ditmar*, the product obtained from α-methylthiophene is α-methylbutadiene and not isoprene.



Polymerization of Butadiene and its Homologues

All the processes of synthesising caoutchouc consist in polymerizing isoprene, butadiene, or similar compounds containing the grouping C:C·C:C.

The polymerization can be effected in a variety of different ways, some of which have been known for many years, and others of quite recent date. The more important of these methods are:—

1. Autopolymerization when kept in a sealed tube (*Tilden*, Chem. News, 1892, **65**, 265; *Weber*, J. Ind. 1894, **13**, **11**; *Harries*, B. 1915, **48**, 683).

2. Under the influence of light (*Wallach*, *A*. 1887, **238**, 88).

3. By raising the temperature to 100°–150° for three days (*Heinemann*, Eng. pat., 1907), or by working at temperatures under 250° (*Hofmann* and *Coutelle*, Ger. pat. 1909). At 100° dimethylbutadiene yields much rubber, but at 150° little rubber and much dimeride (*Kondakoff*, 1909).

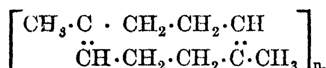
4. Under the influence of chemical reagents.

(*a*) By means of concentrated hydrochloric acid, or a little gaseous hydrogen chloride (*G. Bouchardat*, Bull., 1875, **24**, 108; C. R., 1879, **89**, 361, **1117**; *Tilden*, J. C. S. 1888, **45**, 411).

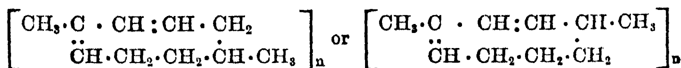
(*b*) Acetic acid for eight days at 100° (*Harries*, 1910). This method is applicable to all butadiene derivatives. It has been suggested that the acetic acid acts as a solvent, and the

polymerization is due to the increase in temperature. The yield is best when pure isoprene is used, and with a temperature of 100° the product is quite white, is readily attacked by oxygen, and can be vulcanized.

In polymerization by the acetic acid method other products are dipentene, an open chain terpene, probably di-isoprene, $CH_2:C(CH_3)\cdot CH_2\cdot CH_2\cdot CH:C(CH_3)\cdot CH:CH_2$, and other dimerides. The amounts of these are less with pure isoprene, and tend to increase with the temperature used. The vulcanization also proceeds most readily with products obtained at the lower temperatures. The products obtained by heating, or, in the case of isoprene, by the acetic acid process, appear closely to resemble natural caoutchouc. That is, the structure of the complex $C_{10}H_{16}$ appears to be the same in both. This has been established to a large extent as the result of *Harries'* experiments. There is a close similarity as regards percentage composition, products of destructive distillation, behaviour with bromine, nitrous acid and ozone, and decomposition products of the ozonides between purified para rubber and the synthetic products. The conclusion is drawn that both contain the grouping—



A careful examination of the products of hydrolysis of the ozonide derived from the synthetic product shows that in addition to the normal products, lævulic aldehyde and its peroxide, small amounts of other products are also formed, one of which appears to be pyruvic aldehyde which indicates the presence of the caoutchoucs, *e.g.*:—



in the synthetic product.

The synthetic product from dimethylbutadiene also appears to yield two isomeric ozonides; on hydrolysis one gives acetonylacetone and the other strongly reducing keto-aldehydes. Whether the value for n in the natural and synthetic caoutchoucs is identical it is impossible to say. Many chemists hold the view that in natural caoutchouc there may be several substances containing the normal octadiene ring but with

different values of n, and the same may hold good for the synthetic products. All attempts to separate, from a latex, rubber of different properties by a process of fractional coagulation have given negative results.

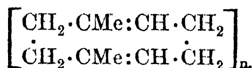
The acetic acid method of polymerization is not so satisfactory as *Hofmann* and *Coutelle's* heat method for isoprene, and when applied to butadiene yields a caoutchouc which has none of the physical properties of ordinary rubber.

(*c*) Metallic sodium, *Matthews*, 1910, *Harries*, 1910. Polymerization occurs when isoprene, or one of its homologues, is kept in contact with about 5 per cent of metallic sodium in sealed vessels; with butadiene a few hours at 35°–40° is sufficient, but with isoprene 50–100 hours at 60° are necessary. The reaction is almost quantitative, no pressure is generated, and no dimerides are formed. The product is very tough, and is sometimes difficult to remove from the autoclaves. It is not identical with natural caoutchouc, and is usually termed sodium caoutchouc or abnormal caoutchouc. The product from isoprene closely resembles para rubber in physical properties; it is very elastic, and vulcanizes well. It yields a solid diozonide soluble in ethyl acetate, and when this is hydrolysed with water or acetic acid only a minute trace of lævulic aldehyde is formed, the reaction of the synthetic product with nitrous acid being also different from that of the natural product.

The presence of caoutchouc appears to accelerate the polymerizing action of sodium on butadiene derivatives. The study of the rate of decomposition of the ozonides is used by *Harries* in deciding between the identity of caoutchoucs prepared by different methods (A. 1913, **395**, 211, 264). Thus the decomposition curves for the products from sodium caoutchouc obtained from isoprene and butadiene are quite different from the curves from natural or normal caoutchouc ozonides. The curves for the diozonides of normal butadiene caoutchouc and $\Delta^{1:5}$ cyclo-octadiene show a marked similarity.

According to *Ostromisslenski* and *Koschelev* (J. Russ. 1915, **47**, 1928) an open chain terpene, β-myrcene, probably CH_2:$CH\cdot C(CH_3)$:$CH\cdot CH_2\cdot CH_2\cdot C(CH_3)$:$CH_2$, is formed when isoprene is cautiously heated at 80°–90°, and this compound with sodium wire at 70°, or with metallic sodium and barium peroxide at 60°–70°, is quantitatively converted into normal caoutchouc, whereas the same reagents convert isoprene into

an abnormal caoutchouc (cf. *Steimmig*, B. 1914, **47**, 350), probably a mixture containing not only 1:5-dimethyl-$\Delta^{1:5}$ cyclo-octadiene, but also the 1:6-dimethyl isomeride—



$$\left[\begin{matrix} CH_2\cdot CMe:CH\cdot CH_2 \\ CH_2\cdot CMe:CH\cdot CH_2 \end{matrix}\right]_n$$

From results of later investigations (J. Russ., 1916, **48**, 1071) *Ostromisslenski* makes the following classification of isoprene caoutchoucs.

α-Isoprene-amylene caoutchouc is obtained from isoprene containing amylene by the action of sodium and is identical with *Matthews*' and *Strange's* and with *Harries*' sodium caoutchouc. The vulcanized product is not elastic, is of no value for industrial applications, and when added to natural caoutchouc lowers the value of the latter. Elementary analysis is insufficient to detect the presence of amylene.

β-Isoprene-amylene caoutchouc is prepared in quantitative yield by the catalytic action of barium peroxide or benzoyl peroxide (p. 475) on the α compound in toluene solution. It forms a compact mass, and at 100° assumes all the elastic properties of natural caoutchouc. It oxidizes readily, and vulcanization converts it into a product which at 80°–90° exhibits all the properties of vulcanized natural caoutchouc.

α-Isoprene caoutchouc is obtained by heating **pure** isoprene with sodium at 60°–70° for 10–40 hours. It is a colourless non-gluey mass, transparent as glass; it swells with solvents, but is not soluble; above 110° it assumes elastic properties. It can be vulcanized and used industrially for certain special purposes.

β-Isoprene caoutchouc is prepared in quantitative yield by the action of sodium with barium (or benzoyl) peroxide on pure isoprene at 60°–70°. It has a pale cinnamon colour and is transparent in thin layers. Its elasticity point is about 80°–90°.

γ-Isoprene caoutchouc. A 40 per cent yield is obtained by the action of barium or benzoyl peroxide or an alkaline sulphide or polysulphide at 45°–50° for 2–4 months. It is a normal caoutchouc in the sense that its elasticity point and fatal temperature are almost identical with those of natural caoutchouc.

δ-Isoprene caoutchouc is the product obtained from β-myrcene (p. 968).

ε-Isoprene caoutchouc. A quantitative yield is obtained by gently heating isoprene with sodium in an atmosphere of carbon dioxide. Its properties are those of a normal caoutchouc.

Recovered caoutchouc is always abnormal with a high elastic point (above 120°), and the process of recovery is accompanied by rearrangement in the nucleus.

Somewhat similar results have been obtained with butadiene. Erythrene under all conditions yields the same polymer.

The conclusion is drawn that the isomerism of α, β, γ, δ isoprene caoutchoucs is conditioned by differences in the positions of the methyl groups, and not by different values of *n* in the complex $(C_{10}H_{16})_n$.

βγ-Dimethylbutadiene, $CH_2{:}C(CH_3)\cdot C(CH_3){:}CH_2$ (p. 962), yields the so-called methyl-rubber by spontaneous polymerization at about 60° for 4–6 months, but the product has properties quite different from those of natural rubber. It oxidizes readily and does not vulcanize easily, but this is partially remedied by the addition of organic vulcanization catalysts, *e.g.* aldehyde ammonia. The methyl-rubber produces vulcanites of good quality.

D. Vulcanization

The production of rubber from caoutchouc or raw rubber is brought about by the process known as vulcanization or curing after the raw rubber has been thoroughly washed and rolled. Technical vulcanization is always effected by the action of sulphur or sulphur chloride, and the object is to improve the mechanical properties of the product so that it may be more serviceable for various purposes, *e.g.* retain its elasticity over a greater range of temperature.

Cold vulcanization (*Parkes*, 1846) consists in dipping thin sheets of raw rubber into a solution of chloride of sulphur, S_2Cl_2, in a suitable solvent, or in exposing the sheets to the vapour of such a solution. The reaction is definitely chemical, and if an excess of a benzene solution of sulphur chloride is used a definite substance, $(C_{10}H_{16})_2S_2Cl_2$, is formed (*Hinrichsen* and *Kindscher*, J. Ind. 1916, **35**, 934). In actual practice a relatively small amount of the chloride is taken up.

Hot vulcanization (*Goodyear*, 1839) is effected by mixing the raw rubber with sulphur, and subjecting the mixture to a temperature of 135°–160°. Various sulphur compounds or

products containing free sulphur have also been recommended The properties of the rubber depend on the degree of vulcanization (state of cure). The elasticity diminishes, but the tensile properties increase up to a certain stage, after which increased vulcanization (*i.e* longer time or higher temperature) produces a brittle rubber which is useless.

A recent method of vulcanization introduced by *Peachey* (E. P. 129826, of 1919) consists in subjecting the raw rubber in the cold, and either in thin sheets or in solution, to the combined action of hydrogen sulphide and sulphur dioxide, the liberated sulphur combining with the rubber (J. Ind. 1921, **40**, 5 T.).

Various theories have been held with regard to the nature of vulcanization. According to *Weber*, the process is chemical and of an additive character, whereas *Wo. Ostwald* (1910) regards the process as purely adsorptive. The modern view is that a certain amount of an additive compound is first formed and that this is then adsorbed into the remainder of the rubber; this view is supported by *Ostromisslenski*'s experiments, which indicate that the vulcanization of raw rubber can be accomplished by adding a small amount of caoutchouc hydrochloride or tetrabromide and subsequently heating. The small amount of additive compound * after, or during, adsorption, produces physical changes in the remainder of the raw rubber, changes which may be accompanied by polymerization.

In practice a mixture containing 5 parts by weight of sulphur and 95 parts of raw rubber is usually taken and vulcanized for a series of gradually increasing periods at a constant temperature (*e.g.* steam under 50 lb. pressure); or in the Netherlands Government Institute 7·5 and 92·5 per cent respectively for 1·5 hours, with steam at 52 lb. pressure. The mechanical properties of the samples are determined, and the period of vulcanization necessary to produce optimum mechanical properties ascertained from the results of the tests.

$$\text{The coefficient of vulcanization} = \frac{\text{combined sulphur} \times 100}{\text{rubber}},$$

the combined sulphur being denoted by the sulphur which cannot be extracted by acetone. According to *Spence*, at optimum cure this value is about 2·8–3, but other authorities give the value 4–5 for rubbers which have the greatest tensile strength.

* According to *Bary* $(C_{10}H_{16})_{20}S_2$ (C. R. 1912, **154**, 1159).

Rubbers containing less than 3 per cent of combined sulphur when kept for 66 hours at 70° often show as high a tensile strength as those obtained by direct cure and containing 5 per cent. This is attributed to ageing, and the conclusion is drawn that the process of curing should vary according to the purpose for which the rubber is required. According to *Stevens* (J. Ind. 1916, **35**, 872; 1918, **37**, 340 T.; cf. *Eaton* and *Day*, ibid. 1919, **38**, 339 T.), if the coefficient exceeds 3·5, appreciable deterioration (as indicated by tensile figures) sets in within twelve months, but no appreciable deterioration is shown in samples with a coefficient of 3·2, so that the period elapsing between vulcanization and testing should be constant, and the temperature during this period fairly constant.

The removal of protein matter from the raw rubber causes the caoutchouc to vulcanize more slowly. This is the main cause in the difference in rates of vulcanization between para rubber and plantation rubber; in the latter case the coagulum is thoroughly washed to remove acetic acid, and this removes most of the protein matter present. According to *Eaton* and *Grantham* (J. Ind. 1915, **34**, 989; 1916, **35**, 715) a rapidly curing rubber of good mechanical properties is obtained if the slabs of coagulum are allowed to stand for six to ten days before further treatment. The cause of this is probably the decomposition of the protein matter by enzymes, and the production of basic nitrogenous products which are not entirely removed by washing or by heating in a dryer. Such caoutchoucs vulcanize in approximately one-third of the time usually necessary for vulcanization.

For Kinetics of Vulcanization, cf. J. Ind. 1918, **37**, 476 A., 595 A.; Com. Netherlands Gov. Inst. 1918, **6**, 799; 1918, **7**, 223.

It is highly probable that synthetic rubber would require the addition of some such accelerator before being vulcanized. (Compare *Ostromisslenski*, J. Ind. 1916, **35**, 58.) Various substances are used as accelerators; of these magnesia, litharge, and lime are the commonest; recently the use of organic bases such as piperidine, diamines, aldehyde ammonia, and various other bases, particularly those with dissociation constants greater than 1×10^{-8} have been recommended. If the bases are too volatile their corresponding carbamides, carbamates, or carbonates can be used. A

solution of potassium hydroxide in glycerol is also a rapid accelerator, but it has been stated that alkalis are injurious, and tend to promote perishing of the rubber, although this has been denied by other chemists.

Ostromisslenski (J. Russ. 1915, **47**, 1462) has recommended *s*-trinitro-benzene as an accelerator, especially in the presence of litharge. Benzoyl peroxide (p. 475) has also been suggested (J. S. C. I. 1916, **35**, 59; cf. also *Colloid Zeitsch.* 1918, **23**, 25). The same author also vulcanizes with similar reagents in the cold, using a metallic oxide or an amine as accelerator.

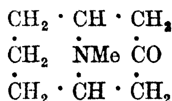
The substance known as vulcanite (cf. p. 971) or ebonite is manufactured by heating raw rubber with larger quantities of sulphur (65:35) for a longer time at higher temperatures. The physical properties characteristic of the rubber are thus completely changed, and a brittle product, probably consisting of compounds $(C_5H_8S)_x$, is formed.

Many rubber goods do not consist simply of vulcanized caoutchouc, but contain fillers. These are added partly to reduce the cost of the rubber and partly to modify its properties for particular purposes; thus mineral matter, such as zinc oxide or magnesia, is usually added when the rubber is required for mechanical purposes involving abrasion and compression; on the other hand, if a colourless eraser is required, a large amount of "white rubber substitute" is added. This substitute is prepared by the action of sulphur monochloride on rape oil. Various materials are also used as pigments. Antimony sulphide is the commonest, and others are yellow sulphide of arsenic, oxide of chromium, zinc chromate, ultramarine, and lamp black. Glue is also used as a filler.

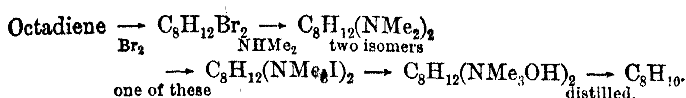
Reclaimed rubber and bitumen are also used for mixing with the rubber. The reclaimed rubber is obtained by reducing old rubber or waste rubber to a fine state of division, treating with acid or alkali, washing with water, and subsequently steaming under pressure in order to render it plastic. Reclaimed rubber, like vulcanized rubber, is insoluble in solvents which dissolve raw rubber; the process of reclaiming does not remove the combined sulphur and frequently only a portion of the fillers present in the waste.

E. The Cyclo-octane Series

The bicyclic ketone pseudopelletierine or methylgranatanine, present in pomegranate peel,



can be reduced to the corresponding CH_2 compound, N-methylgranatanine, by means of zinc dust and dilute sulphuric acid, or by electrolytic reduction in dilute acid solution. The methiodide of N-methylgranatanine with moist silver oxide yields the corresponding quaternary hydroxide, and when this is distilled water is eliminated, the bridge is broken, and **Δ^4-desdimethylgranatanine**, $CH_2<\begin{matrix} CH_2\cdot CH(NMe_2)\cdot CH_2 \\ CH_2\cdot CH:CH—CH_2 \end{matrix}$, is obtained as a colourless oil. When this base is converted into its methiodide, and then into the corresponding hydroxide and distilled trimethylamine, water and **$\Delta^{1:5}$-cyclo-octadiene**, $CH_2<\begin{matrix} CH:CH\cdot CH_2 \\ CH_2\cdot CH:CH \end{matrix}>CH_2$, are formed. The unsaturated compound is a volatile liquid, boiling at 39·5° under 16 mm. pressure, and polymerizes readily, yielding crystalline hydrocarbons. The $\Delta^{1:5}$ structure is ascribed to the hydrocarbon on account of the fact that its ozonide, when decomposed by water, yields succinaldehyde, $CHO\cdot CH_2\cdot CH_2\cdot CHO$, and succinic acid (*Harries*, B. 1908, **41,** 671). A more stable isomeride is obtained by heating the dihydrobromide of the $\Delta^{1:5}$ derivative with quinoline or solid potash. This is a colourless liquid, boiling at 143°–144°, and when reduced by *Sabatier* and *Senderens'* method (p. 675) yields the saturated compound **cyclo-octane,** C_8H_{16}, a colourless liquid with an odour like camphor, boiling at 147°–148° under 709 mm., and melting at 14°. The presence of an eight-membered ring in the compound is confirmed by its oxidation with nitric acid, when a good yield of suberic acid (p. 239) is obtained. A **cyclo-octene,** C_8H_{14}, boiling at 145° and readily polymerizing and a **cyclo-octatriene,** C_8H_{10}, are also known. The latter distils at 36°–40° under 13 mm. pressure, and can be prepared by the following series of reactions:



One of the most interesting derivatives is **cyclo-octatetrene,** C_8H_8, $CH\begin{smallmatrix}\nearrow CH\cdot CH:CH \searrow \\ \searrow CH:CH\cdot CH \nearrow\end{smallmatrix}CH$. A cyclo-octatriene is obtained from N-methylgranatenine in exactly the same manner as cyclo-octadiene from N-methylgranatanine, and this, when subjected to the same series of reactions as described above in the conversion of the cyclo-octadiene into a cyclo-octatriene, yields the monocyclic ring compound, C_8H_8, provided the distillation of the quaternary ammonium hydroxide is conducted under a very low pressure at 30°–45°, otherwise compounds are obtained containing one or even two bridges. It is a yellow liquid with a sweet odour, boils at 42·2° under 17 mm. pressure, has melting-point −27°, and has all the characteristic reactions of olefine compounds. It readily reduces permanganate, absorbs bromine, combines with hydrogen bromide, is readily reduced to cyclo-octane by means of hydrogen and platinum black, and cannot be nitrated or sulphonated. The structure of the molecule is similar to that of benzene, according to *Kekulé* (p. 361), as both consist of a ring of CH groups alternately united by single and double linkings. The complete difference in properties of the two compounds has led *Wilstätter* to reject the *Kekulé* formula for benzene and to accept the *Centric* formula.

Compare B. 1905, **38,** 1975; 1907, **40,** 957; 1908, **41,** 1480; **1910, 43,** 1176; 1911, **44,** 3423; 1913, **46, 517.**

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